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US006217607B1

(12) **United States Patent**
Alt

(10) **Patent No.: US 6,217,607 B1**
(45) **Date of Patent: Apr. 17, 2001**

(54) **PREMOUNTED STENT DELIVERY SYSTEM FOR SMALL VESSELS**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/366,287**

(22) Filed: **Aug. 2, 1999**

Related U.S. Application Data

(63) Continuation-in-part of application No. 09/259,906, filed on Feb. 28, 1999, and a continuation-in-part of application No. 09/175,919, filed on Oct. 20, 1998, now Pat. No. 6,099,561.

(51) **Int. Cl.**[7] **A61F 2/06**
(52) **U.S. Cl.** **623/1.1**; 606/192; 623/1.46
(58) **Field of Search** 606/192, 108, 606/194, 195, 198; 604/96; 623/1.1, 1.44, 1.46

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,645,560 * 7/1997 Crocker et al. 606/192
6,027,517 * 2/2000 Crocker et al. 606/108

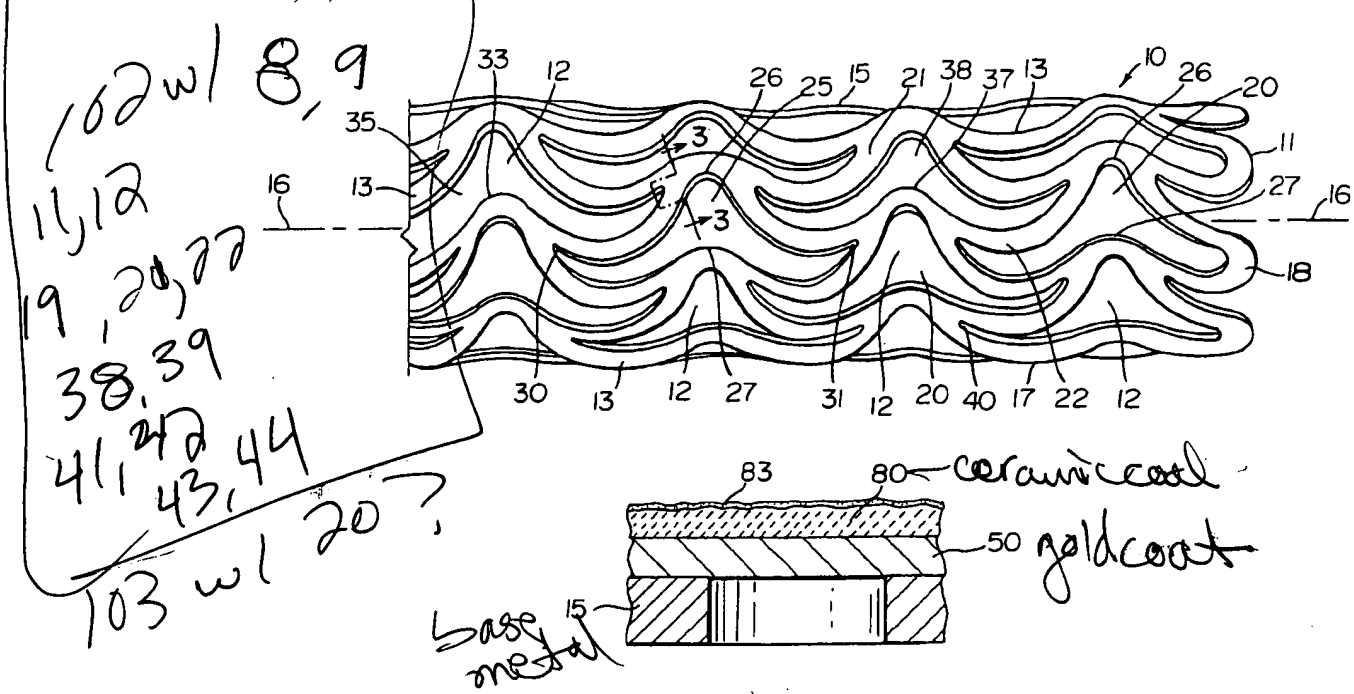
* cited by examiner

Primary Examiner—Kevin Truong

(57) **ABSTRACT**

A stent delivery system is sized to allow it to traverse small-sized vessels of diameter in a range from about 1.25 mm to less than about 2.5 mm in a human body. The delivery system includes a balloon which has an inflated diameter less than 2.5 mm at nominal pressure and is integrated distally on a catheter for selective inflation and deflation through a lumen of the catheter. The stent is adapted to be mounted on the uninflated balloon so that the combination of the balloon when uninflated and the stent mounted thereon has a crossing profile in a range from approximately 0.5 mm to approximately 0.8 mm, to enable the delivery system to rapidly traverse the small-sized vessel for subsequent deployment of the stent at a preselected target site of the vessel. At the target site, the balloon is inflated to expand the diameter of the stent to lodge against the wall of the vessel and remain in place when the balloon is deflated and the delivery system is withdrawn from the vessel. The stent has a coating with a surface feature that increases the retention of the stent on the balloon during advancement of the stent delivery system through the vessel.

18 Claims, 1 Drawing Sheet



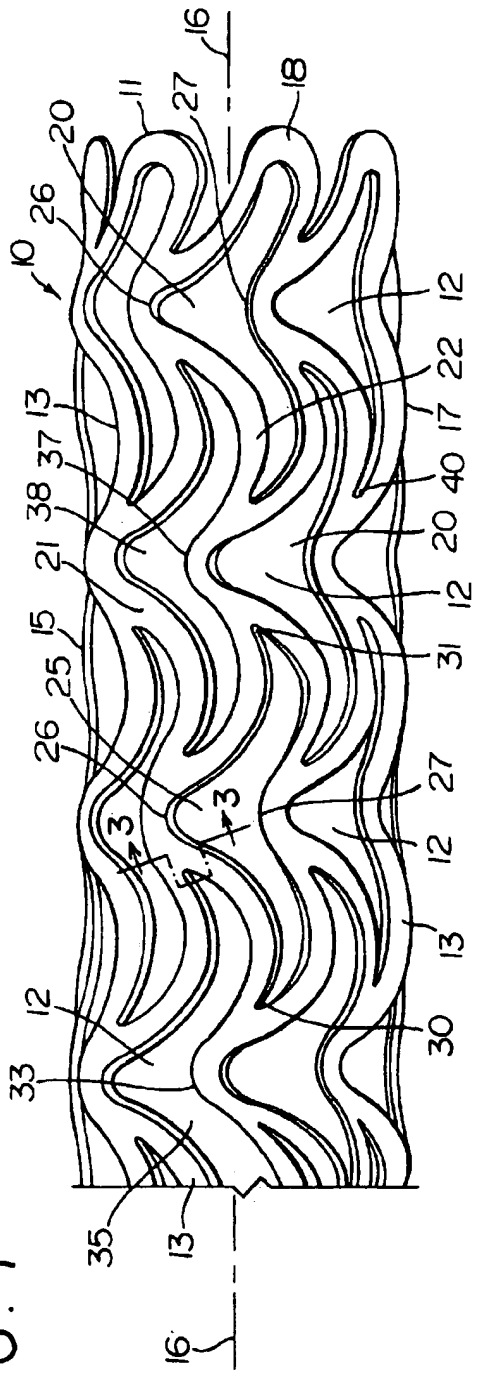


FIG. 1

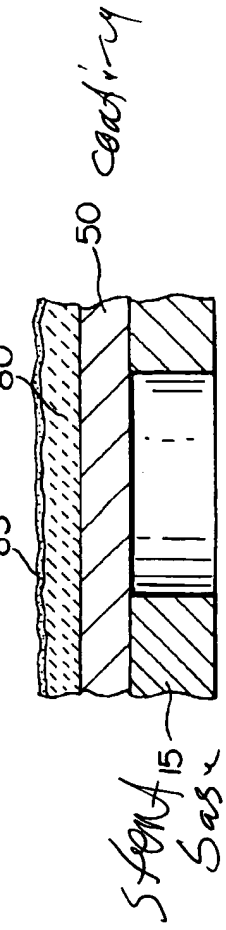


FIG. 3

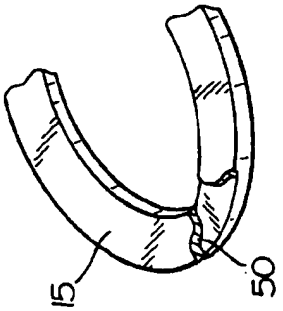


FIG. 2

PREMOUNTED STENT DELIVERY SYSTEM FOR SMALL VESSELS

CROSS-REFERENCE TO RELATED APPLICATION

This application is a continuation-in-part of U.S. application Ser. No. 09/175,919, filed Oct. 20, 1998, now U.S. Pat. No. 6,099,561 and U.S. application Ser. No. 09/259,906, filed Feb. 28, 1999, now pending of the applicant herein, and is assigned to the same assignee as each of those applications.

BACKGROUND OF THE INVENTION

The present invention relates generally to stents which are implantable or deployable in a vascular or endoluminal location within the body of a patient to maintain the lumen open at that location, and more particularly to improvements in stent.

Stents are expandable prostheses employed to maintain narrow vascular and endoluminal ducts or tracts of the human body open and unoccluded, such as a portion of the lumen of a coronary artery after dilatation of the artery by balloon angioplasty. While vascular usage is frequently discussed in this application, it will be understood by those skilled in the art that stents having the characteristics and features of the present invention may be implanted in other ducts or tracts of the human body to keep the lumen open, such as in the cerebral circulation system, tracheo-bronchial system, the biliary hepatic system, the esophageal bowel system, and the urinary tract system

In the case of an occluded coronary artery, for example, the original blockage is typically attributable to fatty deposits or plaque on the inner lining of the vessel. A different mechanism, however, produces a new blockage after an angioplasty procedure is performed to compress the deposits against the inner lining of the vessel, as by use of balloon angioplasty, or to virtually entirely remove the deposits, as by use of laser angioplasty or rotational cutting. The blood vessel wall is subjected to trauma by any of these procedures, which results in hyperplasia of the neointima, i.e., a rapid proliferation of muscle cells in the affected region of the wall, to cause restenosis and re-occlusion of the vessel lumen in a significant percentage of angioplasty patients within a period of from three to six months following the initial procedure.

To avoid this re-occlusion and to maintain the lumen of the vessel open, it is customary procedure to install a stent at the site in the vessel where the angioplasty was performed. The stent is deployed by radial expansion under pressure exerted by the inflating balloon of a balloon catheter on which the stent is mounted, to engage the inner lining or surface of the vessel wall with sufficient resilience to allow some contraction but also to provide a degree of stiffness to resist the natural recoil of the vessel wall following expansion.

Trends and extensions of increased knowledge and methods in practical cardiology are based primarily on advances in basic science and applied technology. For example, ten years ago, treatment of myocardial infarction (GI) stressed limiting physical injury and damage and focused principally on rehabilitation. The treatment strategy for acute MI was followed by a period of use of a thrombolytic agent. New techniques, new catheters, new stents and guidewires and improved fluoroscopic x-ray machines have more recently enabled treatment of acute MI with interventional catheter techniques. In one of these techniques, involving an angioplasty procedure, a small guidewire is advanced through an occlusion of a coronary artery which is attributable primarily to a thrombus, a balloon catheter is then advanced along the guidewire, and the balloon is inflated at the site of the thrombus to open the lumen of the artery. A stent is deployed at the lesion site either concurrently with or immediately following the angioplasty procedure to provide the necessary mechanical support to hold the lumen of the dissected vessel wall open.

This technique has been applied very successfully in coronary vessels which have a range of diameters from approximately 2.5 to 3.5 millimeters (mm). However, present day successful treatment of vessels having diameters smaller than 2.5 mm remains quite limited, because currently available apparatus and stent delivery systems are inadequate to negotiate such small vessel sizes to allow installation therein.

A wide clinical spectrum of diseases exists that would be receptive to beneficial treatment of vessels smaller than 2.5 mm in diameter. One such instance is treatment of side branches of the coronary arteries, which has a beneficial indication. A capability to treat vessels other than coronary vessels but of similarly small diameter, such as vessels enabling blood circulation in the brain, would likewise be desirable.

Ischemic stroke is characterized by pathophysiological characteristics which are very similar to those of MI. An artery is occluded either by an embolized thrombus as in patients with atrial fibrillation, or by a local thrombus that builds up on an arteriosclerotic vessel wall. Often these arteriosclerotic vessels are undergoing a local dissection, which limits the blood flow and activates the coagulation system. Access to small occluded arteries of the brain or other parts of the body for implementing procedures to allow adequate blood flow therethrough is a highly desirable objective for treating millions of persons likely to suffer stroke each year.

One of the technical prerequisites for successful treatment in these respects is the availability of a stent, and related delivery system, which is sufficiently small and thin that it can navigate and be and deployed in these tiny vessels without occluding the lumen thereof It is also essential that the stent be highly visible during and after implantation to enable proper deployment and aftercare by the physician. The latter attribute is especially important for treatment of intracerebral arteries, because of the obstacle to x-rays presented by the skull which makes precise visualization of a small thin stent extremely difficult. The stent should, therefore, be sufficiently radiopaque for valization without need for its struts to be made so large that the stent itself creates an unacceptable obstruction of the lumen of the vessel.

Another prerequisite of a successful treatment of these extremely small diameter vessels is that the stent delivery system should be highly flexible to allow it to be advanced along the anatomy of the cerebral circulation.

In addition, the total stent delivery system must be of extremely small profile, which will allow vessels of 2.0 mm, 1.75 mm or even 1.50 mm diameter to be addressed. No currently available stent delivery system has a balloon with a diameter less than about 2.5 mm when inflated at nominal pressure.

Therefore, it is a principal aim of the present invention is to provide stents and stent delivery systems having such attributes and characteristics, so as to enable successful treatment of extremely small diameter blood vessels and

other ducts, tracts or conduits of the human body, without unacceptable obstruction of the vessel lumen itself.

SUMMARY OF THE INVENTION

According to the present invention, a stent and a stent delivery system are provided with features and characteristics which will allow the stent to be premounted on the balloon of the delivery system for easy introduction into and advancement through vessels having diameters in a range from about 1.25 to less than 2.5 mm. The solution to achieving these ends lies in implementing a suitably small-sized stent.

It is crucial in the case of a very small-sized stent, as with the present invention, that there be sufficient retention force between the stent and the balloon that the stent will be maintained in place on the balloon. This retention must exist throughout travel of the stent, so as to avoid having the stent dislodged from the balloon during navigation of the delivery system through the vessel. At the same time, the stent must—despite its small crossing profile which will avoid innate obstruction of the vessel lumen—possess sufficient mechanical strength to support the vessel wall at a target site where it will be deployed. Further, it must resist the natural recoil of the vessel wall which inevitably follows deployment of the stent.

Added to these prerequisites is the further need to maintain sufficient visibility of such a small-sized stent that the implanting physician is able to properly place the stent for deployment to successfully carry out the procedure.

Ordinarily, for mounting or premounting, the stent is crimped onto the balloon under external pressure. Consequently, the mesh structure of the stent undergoes considerable deformation during the crimping procedure, which takes two individual and distinct forms. First, the stent undergoes an elastic deformation in response to the external pressure applied to crimp it to a smaller diameter. In this type of deformation, the stent assumes a new shape but, because of its elastic properties, seeks to return to its former shape—even if only slightly—when the external pressure is removed. Second, the stent undergoes plastic deformation which tends to maintain the new shape that resulted from the external pressure of crimping. The greater the plastic deformation compared to the elastic deformation—i.e., the higher the ratio of the former to the latter—the higher is the retention force exerted by the stent on the balloon. As noted above, maximizing or optimizing this retention force is an important aspect of the invention.

Another important consideration in implementation of an embodiment of the present invention is the reduction of outside or exposed surface area of the balloon used in the stent delivery system, that occurs with reduction of the balloon diameter to accommodate a much smaller stent than is ordinarily encountered. For the small stent size of the present invention, the uninflated balloon diameter preferably ranges from about 0.5 to about 1.0 mm, and more preferably from about 0.5 mm to about 0.8 mm. The resultant relatively small outside surface area of the balloon has a further deleterious effect on retention force exerted by the stent when mounted in crimped fashion on the balloon.

Therefore, it is another important aim of the present invention to provide a premounted stent delivery system suitable for traversing body vessels, ducts or tracts having lumen diameters in a range from about 1.25 mm to less than about 2.5 mm, in which the stent exhibits a very high retention force despite the small diameter of the stent and the delivery system balloon and the relatively small outer surface area of the balloon.

According to the invention, the stent is provided with a rough surface characteristic, rather than a smooth surface as is typical for stents, and this rough surface characteristic or feature significantly increases the retention force of the stent on the balloon. A coating material is applied whose inherent material characteristics serve to increase the surface structure and area of the basic stent to which it is applied or on which it is formed. Such a surface characteristic is provided, for example, by the techniques and methods described in co-pending U.S. patent applications Ser. No. 09/059,053 and Ser. No. 09/175,919 of the applicant herein, assigned to the same assignee as the present application. The finished stent has a multi-layer surface region, the outer layer being a ceramic-like material with a relatively rough external surface. This outer layer is biocompatible and may be very thin, with the composition of a compound or derivative of certain metals such as iridium oxide (sometimes referred to herein as "IROX") or titanium nitrate. The outer layer overlies the entire exposed surface of the stent, so that when the stent is mounted on and crimped against the balloon of the stent delivery system, the rough surface structure of the stent lumen resides directly against the outer surface of the balloon along the area of contact. The surface roughness, however, is not so extreme as to potentially puncture the balloon. Creation of a rough surface may be achieved by a number of alternative techniques, beyond those disclosed in the aforementioned '053 and '919 applications, examples of which will be described in the detailed description below.

In a preferred embodiment, the multi-layer stent is composed of three different layers including an innermost tubular core, an intermediate corrosion-resistant layer overlying the core material, and the aforementioned thin ceramic-like metal or derivative thereof outer layer overlying the intermediate layer and providing the rough surface characteristic of the overall stent. In an exemplary embodiment, the core material is medical grade stainless steel, the intermediate layer is gold, and the outer layer is IROX. It is important that each of the intermediate and outer layers tightly adhere to its respective directly underlying layer material. Tight adherence of the gold coating to the underlying steel core may be achieved, for example, by a process described in U.S. Pat. No. 5,824,045, which is assigned to the assignee of the present application. The noble metal layer (e.g., gold) aids both in keeping the total thickness of the stent relatively small, while considerably enhancing the visibility of the stent on x-ray fluoroscopy over the visibility of a correspondingly thin layer of steel, for example, to aid the implanting physician in guiding the stent to and deploying it at a desired target site in the vessel.

The core material of the stent is generally constructed of an elongate biocompatible metal member composed, for example, of 316L stainless steel (medical grade), but may alternatively be composed of other biocompatible material such as titanium, Nitinol (nickel-titanium alloy with shape memory characteristics), iridium, or other metal, which is configured in an open-ended tubular or cylindrical shape (e.g., coil, mesh, undulating single wire filament or perforated tube). For convenience, the portion of the stent between its open ends is referred to herein as the sidewall, regardless of the particular tubular shape of the structure, and as having openings therethrough even though a coil stent has only one continuous spiral opening in its sidewall and a continuous filament wire may have very large openings in its "sidewall."

When mounted on the balloon, the stent of the present invention is of sufficiently small diameter—with a total crossing profile of from 0.5 to 0.8 mm, depending on final

size—to be accommodated by and to readily traverse a vessel, tract or other duct of patient's body less than 2.5 mm in diameter, and optimally between 1.25 mm and 2.5 mm, to the site at which the stent is to be deployed. The rough outer surface of the stent serves to increase the retention force of the stent when crimped on the balloon, for secure retention of the stent and ease of navigation of the stent delivery system through the vessel. Deployment is achieved by controlled inflation of the balloon of the stent delivery system to apply a uniform radial outwardly directed force on the sidewall of the stent to increase its diameter, and thereby expand or open the stent until it is in firm contact or engagement with the inner lining of the vessel wall, for retention at that site. The mechanical strength of the stent should be adequate to resist collapse from the natural recoil of the vessel wall when the balloon is deflated and the delivery system is withdrawn from the patient's body.

Thus, despite a smaller area of contact between the stent and the balloon of the delivery system, a high retention force is created as a consequence of the increased friction between them owing to the relatively rough surface of the stent. There is no need for taking special pains for fitting or aligning components or for increasing the diameter (which could defeat the desire to navigate the small-sized vessels), and even balloons that are normally used solely for balloon angioplasty will suffice for use as the balloon of the stent delivery system.

Another problem typically encountered in stent delivery systems sought to be used in small-sized vessels is that the sidewall thickness of the stent has been made relatively large in an effort to achieve improved retention force on the balloon. But a large wall thickness undesirably reduces the lumen diameter of the vessel at the site of deployment of the stent. For to example, in a vessel of 1.50 mm lumen diameter, a stent with a wall thickness of 0.125 mm results in a lumen diameter reduction of 0.25 mm, i.e., a loss of almost 17% in total lumen diameter. In the stent delivery system and method of the present invention it is possible to use a stent having a wall thickness of much smaller dimension—in a range on the order of only 50 microns (micrometers, or μm) to 75 μm—and thereby, with considerably less adverse effect on vessel lumen diameter. This is because the increased friction attributable to the rough surface of the stent compensates for the lower retention force attributable to the reduced sidewall thickness of the stent.

BRIEF DESCRIPTION OF THE DRAWINGS

The above and still further aims, objectives, features, aspects and attendant advantages of the present invention will become apparent from the following detailed description of preferred embodiments and methods of manufacture and usage of a stent and a delivery system on which the stent is premounted, constituting the best mode presently contemplated of practicing the invention, when taken in conjunction with the accompanying drawings, in which:

FIGS. **1** and **2** are, respectively, a perspective view of an embodiment of a vascular or endoluminal stent having a rough surface structure according to the present invention, and a relatively enlarged partially-processed fragmentary portion thereof; and

FIG. **3** is a cross-sectional view of a three-layer preferred embodiment of the stent of FIG. **1**.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENT AND METHOD

Each of the '919 and '906 applications is incorporated in its entirety into this specification by reference. Nevertheless, for the sake of convenience to the reader, certain portions of the two co-pending applications will be repeated in some detail herein.

In FIG. **1** (not to scale) stent **10** is fabricated as a hollow tubular self-supporting structure or member **11** composed of a biocompatible metal such as medical grade 316L stainless steel, although other metals may alternatively be used, such as titanium, iridium, or Nitinol, for example. The tubular member is provided with a multiplicity of through-holes or openings **12** through sidewall **15**, defined and bounded by a plurality of struts or links **13**, which enables expansion of the stent diameter when the device is to be deployed at a target site in a vessel, duct or tract of the human body. The openings **12** may be precisely cut out to form a latticework sidewall using, for example, a narrow laser beam following a programmable pattern. The removed material is discarded.

By way of example, the resulting pattern in the latticework sidewall **15** is a network of interconnected struts **13** which are optimized for orientation predominantly parallel to the longitudinal axis **16** of the tube **11**, with none of the struts oriented perpendicular (i.e., transverse) to the axis **16**, so that no strut interconnecting any other struts in the latticework is oriented to lie completely in a plane transverse to the longitudinal axis, without running from one end of the stent to the opposite end. This structure, described in detail in applicant's copending application Ser. No. 08/933,627, also incorporated by reference in its entirety herein, provides a very low friction characteristic (or coefficient of friction) of the outer surface **17** of the stent, to ease advancement of stent **10** in a vessel, duct or tract to a site for deployment.

The network or latticework of struts **13** defines a series of longitudinally repeating circumferential rows of openings **12**. Each pair of struts such as **21, 22** bounding an opening **12** in any given row **25** are in the shape of circumferentially displaced wavelets with adjacent circumferentially aligned higher and lower crests **26, 27**, respectively, in which the wavelets intersect (**30**) one another at one or both sides of the crests (**30, 31**). The intersection **30** of struts (or wavelets) at one side of the adjacent circumferentially aligned crests **26, 27** of row **25** is tangential to a crest **33** of the immediately adjacent row **35**, and the intersection **31** of struts (or wavelets) at the other side of those crests is tangential to a crest **37** of the immediately adjacent row **38**. Interconnecting points such as **40** between the struts may be notched to enhance symmetrical radial expansion of the stent during deployment thereof

When the stent **10** is crimped onto a small diameter (low profile) delivery balloon (not shown), the adjacent circumferentially aligned crests of each row move closer together, and the pattern formed by the latticework of struts allows substantial nesting together of the crests and bows, which assures a relatively small circumference of the stent in the crimped condition. This stent is highly flexible, and is capable of undergoing bending to a small radius corresponding to radii of particularly tortuous coronary arteries, without permanent plastic deformation.

As the stent **10** is partially opened by inflation of the balloon during deployment, the adjacent crests begin to separate and the angle of division between struts begins to open. When the stent is fully expanded to its deployed diameter, the latticework of struts takes on a shape in which adjacent crests undergo wide separation, and portions of the struts take on a transverse, almost fully lateral orientation relative to the longitudinal axis of the stent. Such lateral orientation of a plurality of the struts enables each fully opened cell to contribute to the firm mechanical support

offered by the stent in its fully deployed condition, to assure a rigid structure which is highly resistant to recoil of the vessel wall following stent deployment. It bears emphasis, however, that the configuration of this stent structure, while highly desirable, is illustrative only and not essential to the principles of the present invention.

The tubular steel core sidewall **15** of the stent is coated with a thin, tightly adherent layer **50** (FIG. **2**, a fragmentary perspective view shown partly in section for clarity) of noble metal, preferably gold, but alternatively an alloy which is primarily composed of gold or other noble metal. The gold layer is applied to cover the entire exposed surface of the basic metal stent, whether of the type shown, or a metal mesh, or other configuration. This is preferably but not necessarily achieved by a method described in the aforementioned '045 patent, which is incorporated in its entirety herein by reference. Preferably, this layer has a thickness in a range from 1 μm to 10 μm, and more preferably about 5 μm.

According to the latter patent, the thin adherent film or layer **50** of gold is applied by a process of ion beam deposition to provide a firm, tightly bonded, extremely thin foundation layer, which allows the bond between base metal and noble metal to flex without suffering fracture or peeling of the overlying layer. This initial foundation layer is built upon preferably by a conventional galvanic process by which one or more additional thin, tightly adherent uniform layers of gold are applied, to form an overall composite layer of gold having a thickness of from about 3 μm to about 6 μm, and preferably about 5 μm, on each side of the wall of the stent. The overall effect of these processes is a layer adherence that precludes cracking, peeling or flaking of any portion of the overall gold layer from the underlying surface of the steel core, which might otherwise occur during times when the stent is undergoing mechanical stress and distortion, such as during pre-opening, crimping, and expansion-during deployment phases of the procedure.

Stent **10** preferably is composed of three different primary or fundamental layers as shown in the greatly exaggerated fragmentary cross-sectional view of FIG. **3**, taken through the line **3**—**3** of FIG. **1**. By "primary" and "fundamental", as used here, it is meant that although the stent may have additional layers, coatings or films, the three layers—two of which have been described thus far—are important to the favorable characteristics enjoyed by the stent.

The third or upper or outermost layer **80** is preferably composed of a ceramic-like metal material such as either iridium oxide (IROX) or titanium nitrate, these materials being exemplary of a biocompatible layer that serves a primary purpose of avoiding tissue irritation and thrombus formation. This outermost layer may be deposited as an inert coating over the surface(s) of the underlying intermediate noble metal layer by any known method, preferably to a thickness in the range from about 500 nm to about 1,500 nm (=1.5 μm). This outermost layer is also preferably applied to all exposed surfaces of the wall of stent **10**, so it is the surface that contacts both the inner lining of the vessel and the blood flowing through the lumen of the vessel in which the stent is implanted (deployed).

In addition to assuring the absence of a galvanic potential that could cause corrosion of the base layer, the intermediate noble metal layer serves to enable flexing of the stent over a vast number of cycles encountered in actual use without loss of the overlying rough surface coating (outermost layer) from flaking, shedding or disintegration.

A high voltage sputtering process is among many suitable processes that may be used to form this outermost rough surface coating. Others include anionic oxidation, thermal oxidation, sintering, and electrodeposition. Oxalic acid, application of current and heat, and additional use of an ultrasound bath have been found to produce a very tight adhesion of iridium oxide to the underlying intermediate layer. Suitable processes for forming iridium oxide or titanium nitrate layers also have been developed and can be performed by Hittman Materials & Medical Components, Inc. of Columbia, Md., for example. In any event, the outermost layer **80** is formed with a relatively rough surface, for purposes of providing the increased friction factor and retention force according to the present invention.

A three layer stent structure can be produced with an overall thickness in a range from about 50 μm to about 75 μm. The stainless steel wall may be fabricated in a thickness of approximately 45 to 60 μm, which offers sufficient mechanical strength to resist the natural recoil of the blood vessel wall following deployment of the stent. The gold intermediate layer is applied in a 5 μm thickness, for example, to all exposed surfaces of the base layer, giving a total additional thickness of about 10 μm to the structure, and serving to avoid a galvanic potential. The outermost layer of iridium oxide is formed to a thickness preferably in a range from 500 nanometers (nm) to about 1.0 μm.

The most preferred method of producing the outermost stent coating of iridium oxide is described in detail in the '906 application. Briefly, the method employs a combination of a chemical bath process together with application of heat and mechanical forces. An ultrasonic water bath is maintained at a preselected water temperature according to the setting of a thermostat. Initially, the surface of each stent to be coated is prepared by activation. For a gold-coated stent with a base or core metal of medical grade stainless steel, iridium, titanium or Nitinol, for example, adequate surface activation is achieved by immersing the stent in a solution of 10% oxalic acid at a temperature of about 100° C., for a period of about 30 minutes. The stents are then thoroughly rinsed with distilled water and dried in air at a laminar flow at room temperature. Each stent is then inserted into a respective glass vial for the coating process, and the vials are then inserted into respective holders of a tray or trays for partial submergence in the water bath.

A quantity of coating solution is added to the vial sufficient to cover the stent. The coating solution is prepared by dissolving 200 milligrams (mg) of iridium chloride in 5 ml of 20% hydrochloric acid, in a separate reaction beaker, then boiling slowly at approximately 100° C. until the solution is evaporated to approximately 20% of its original volume, e.g., from 5 ml to one ml. Although the coating solution may be stored, it is preferably used within seven days after having been prepared. 500 microliters (μl) of coating solution was found to be sufficient for full coverage of the stent for a vial with a liquid content capacity of one milliliter (ml), but the amount of coating solution to be added to a vial for a particular stent will depend on and be adjusted according to the size and surface dimensions of the stent to be coated. Each vial is closed with a stopper having a tiny hole for pressure relief during operation of the bath.

In the bath, the vials are arranged in the holder such that each is upright and the entire stent lies completely below the bath water level. In an exemplary operation of the bath, the ultrasonic generator delivered a mean energy of 320 watts at a frequency of 35 kiloHertz (kHz). The vials and stents undergo vibration at that frequency, and the water bath undergoes heating up to the preset temperature, which is maintained by virtue of circulating coolant water at the exterior of the bath, while continuously maintaining the ultrasonic vibrational energy for adherence of the coating.

During the ultrasonic bath operation, the iridium chloride in the coating solution substantially uniformly coats the submerged stent with a layer of iridium chloride, which is ultimately converted to iridium oxide during retention of the vials in the bath in the presence of heat, ultrasonic energy, and air. Any molecular bound water leaves the crystal structure of the iridium oxide following the heating.

After a period of time—at least about 6 hours of bath operation in an exemplary procedure—the vials are removed from the bath, and the stents are then removed from the vials, rinsed with de-ionized pure water, and dried in a laminar flow of air for about one hour at room temperature. This is followed by heating the coated stents in an oven for about 12 hours at a temperature of 320° C. The heating converts any residual iridium chloride in the coating to iridium oxide, so as to create the final complete iridium oxide coating. Then the stents are cleaned ultrasonically and with alcohol in a manner which is customary for biomedical implants.

Stents averaging 16 mm in length, with a diameter suitable for mounting on an uninflated balloon of a diameter from about 0.5 to 1.0 mm and a strut thickness of from about 50 to 75 μm underwent a slight increase in weight which depended on the desired coating thickness. A coating thickness ranging from about 500 nm to about 1 micron maybe optimum.

Tests conducted on stents coated by this method including vibrational, ultrasonic, bench and maximum expansion/repeated crimping tests—have demonstrated that the iridium oxide is firmly attached to the underlying base or core metal of the stent, so this outer layer will neither flake off nor disintegrate from the stent even with maximum expansion during subsequent implantation and deployment. It is believed that by the continuous application of ultrasonic energy in the coating method, only those iridium oxide molecules that attach to the underlying base metal enter into a very firm bond, while the other molecules are removed from the stent and, with the ultrasonic induced vibration, are dissolved in the prepared solution.

The thickness of the iridium oxide layer which is formed on the base metal of the stent, and the roughness of its exposed surface, are controlled by appropriate variation of the iridium compound and its amount and concentration in the prepared solution, as well as by the characteristics of the ultrasonic bath. A relatively rough outer surface on the firmly bonded iridium oxide layer, and thus of the overall stent itself provides numerous indentations.

The rough outer surface serves to increase the coefficient of function and the retention force of the stent when mounted on a balloon for implantation in a small-sized vessel of the human body. A considerable risk exists that a balloon catheter-mounted stent might be dislodged from the uninflated or partially inflated balloon as a result of navigation through the tortuous path of the cardiovascular system or other vessels of the body to the preselected site for deployment, particularly if the stent surface is smooth and/or the stent thickness and diameter are small. The rough surface of the outer layer provides the stent with high retention force, exceeding 2.5 Newton, even where less mechanical grip exists because of thin stent strut thickness, and the stent is mounted on a small diameter (e.g., <1.0 mm, uninflated) balloon.

Other techniques may alternatively be used for forming a relatively rough outer surface on the stent, suitable for purposes of the present invention. For example, the surface may be treated to electropolishing in which an acid is applied or added to the bath, and a predetermined current of several amperes is applied, so as to create a rough rather than a smooth surface. Or, metal particles may be sputtered onto the metal surface of the stent, such as stainless steel 316L particles sputtered onto a 316L stent surface, to increase the surface roughness. Or, the stent may be cut from a rough and porous tubing using techniques which have been implemented by the aforementioned Hittman company. These examples are merely illustrative, not exhaustive.

Although the iridium oxide coating on the stent is an inorganic biomaterial, it exhibits an ability to reduce the degree of inflammation which could otherwise occur when such biomaterial contacts the human body. Normally, an inorganic biomaterial is a passive structure with only passive mechanical properties. But it has been found that iridium oxide produced by the preferred method herein has catalytic properties, capable of promoting a reaction in which hydrogen peroxide (H_2O_2) is converted into water (H_2O) and oxygen (O_2). This reaction normally occurs only in the presence of a catalyst, since hydrogen peroxide is normally kinetically stable and will not decompose spontaneously. To become unstable, a certain kinetic energy is required to overcome the activation energy for hydrogen peroxide decomposition.

It is known that one of the very first responses of the human body to the implantation of a foreign body, such as a stent surface, into the blood vessels is the activation of leukocytes, white blood cells which are one of the formed elements of the circulating blood system. This activation causes oxidative stress with a burst of reactive oxygen compounds (100 times higher than the baseline production). One of the key molecules in this process is hydrogen peroxide, released by neutrophilic granulocytes which constitute one of the five types of leukocytes. While O_2 is always present and generated in a normal cell cycle, in the mitochondria the reaction of O_2 to superoxide anion O_2 (i.e., reactive form of oxygen when molecular oxygen gains a single electron) is reduced to H_2O_2 by the enzyme superoxide dismutase. The enzyme catalase serves as a converter of H_2O_2. The presence of H_2O_2 is a very strong trigger for inflammation. And in a situation where inflammation is occurring, when the granulocytes produce 100 times more O_2 than normal, the normal catalytic activity of the body is insufficient to convert the increased amount of H_2O_2 to water and oxygen in its metabolic process. It has been found that this iridium oxide surface of the stent, though a primarily passive structure, is a biologically active surface which is highly effective in preventing inflammatory reactions. The presence of catalytic properties of an otherwise biologically inactive surface of this biomaterial appears to be partly attributable to molecular adherence of the iridium structure as discussed above, and partly attributable to the porous surface structure of the iridium oxide layer, which enables the stent to be implanted without significant inflammation.

It will be observed that the stent delivery system, method of assembly, and stent of the present invention provides sizing to allow the stent delivery system to traverse small-sized vessels of a human body, nominally ranging in diameter from about 1.25 to less than about 2.5 mm. The delivery balloon has an uninflated diameter considerably less than 2.5 mm, and indeed less than 1.0 mm, ideally from about 0.5 to 0.8 mm, integral with the catheter distally thereof i.e., at or near the distal end of the catheter, through which the balloon may be selectively inflated and deflated via an inflation lumen of the catheter. The stent is adapted to be firmly but removably mounted on the uninflated balloon, as by crimping thereon, and typically is premounted in that way for use

by the implanting surgeon upon removal of the delivery system from its package. The overall diameter of this assembly and its crossing profile preferably lies in a range from about 0.5 mm to about 0.8 mm. One of the stent and the balloon includes a feature for increasing the retention force between the stent and the balloon while the stent is mounted on the balloon, so that the stent is held securely in place as the stent delivery system is navigated through the vessel.

According to the preferred embodiment, that is the function of the stent's outer rough surface. It is also possible, however, albeit not preferable, within the confines of the invention, to provide a surface feature of the balloon to achieve that end, or to apply a medical grade biodegradable biomaterial adhesive to the portion of the balloon surface on which the stent is to be mounted. But an adhesive may prevent release of the balloon after the stent is deployed.

Although certain methods and embodiments of the invention have been disclosed herein, it will be recognized from a consideration of the foregoing description that variations and modifications may be made without departing from the spirit and scope of the invention. Accordingly, it is intended that the invention shall be limited only by the appended claims and the rules and principles of applicable law.

What is claimed is:

1. A small profile stent delivery system for traversing small vessels of less than about 2.5 mm diameter of a human body, comprising a catheter having a balloon integrated distally on said catheter for selective inflation and deflation via an inflation lumen of said catheter; a stent firmly mounted on said balloon for traversal of a said small vessel by the delivery system and subsequent deployment of said stent at a preselected target site of the vessel by inflation of said balloon to expand the diameter of said stent to lodge against the inner wall of the vessel; said balloon having an optimum inflated diameter less than about 2.5 mm at nominal balloon pressure of from about 6 atmospheres (atm) to about 8 atm; one of said balloon and said stent having a non-adhesive intrinsic surface region characteristic implemented to enhance the retention force between said balloon and said stent mounted thereon to prevent said stent from being dislodged from said balloon as the delivery system traverses a said small vessel despite the small profile of the delivery system but to permit said stent to be released from said balloon and remain lodged against the inner wall of the vessel after deployment at the target site and deflation of said balloon and removal of said catheter from the vessel.

2. The small profile stent delivery system of claim **1**, wherein said balloon when substantially uninflated with said stent mounted thereon for traversal of a said small vessel, together have an overall diameter and crossing profile in a range from approximately 0.5 mm to approximately 0.8 mm.

3. The small profile stent delivery system of claim **1**, wherein said non-adhesive intrinsic surface region characteristic substantially increases the friction between said balloon and said stent mounted thereon relative to an absence of said characteristic.

4. The small profile stent delivery system of claim **3**, wherein said non-adhesive intrinsic surface region characteristic comprises a rough surface of said stent along at least the surface of said stent in contact with said balloon when said stent is mounted on said balloon.

5. The small profile stent delivery system of claim **4**, wherein said rough surface of said stent comprises a layer of ceramic-like material adherently overlying the entire surface of said stent.

6. The small profile stent delivery system of claim **4**, wherein said rough surface of said stent comprises a layer of material selected from a group consisting of iridium oxide and titanium nitrate adherently overlying the entire surface of said stent.

7. The small profile stent delivery system of claim **6**, wherein said stent has a total sidewall thickness in a range from about 50 μm to about 75 μm.

8. The small profile stent delivery system of claim **6**, wherein said delivery system has a crossing profile sized to traverse vessels having a lumen diameter in a range from about 1.5 mm to less than 2.5 mm.

9. A method of assembling a small profile stent delivery system for traversing small-sized vessels of less than 2.5 mm diameter in a human body, comprising the steps of selecting a balloon catheter with an integral distal balloon having an optimum inflated diameter less than 2.5 mm at nominal balloon pressure of from about 6 atmospheres (atm) to about 8 atm wherein said balloon is selectively inflatable and deflatable through an inflation lumen of said catheter; mounting firmly on said balloon a stent having a non-adhesive intrinsic surface region characteristic along its surface adapted to reside against the surface of said balloon to enhance the frictional force and thereby the retention force between said balloon and said stent mounted thereon whereby the combination of said balloon when uninflated and said stent mounted thereon has an overall diameter and crossing profile in a range from approximately 0.5 mm to approximately 0.8 mm and said stent delivery system is equipped to traverse a said small-sized vessel without dislodging said stent from said balloon during advancement to a preselected target site and to freely release said stent from said balloon upon deployment of said stent against the vessel wall at said target site and deflation and withdrawal of said balloon from the small-sized vessel.

10. The method of claim **9**, including the step of forming said non-adhesive intrinsic surface region characteristic of said stent by roughening the surface of said stent at least along an area adapted to contact said balloon.

11. The method of claim **10**, wherein said roughening step includes forming an adherent surface layer comprising a ceramic-like material overlying said stent.

12. The method of claim **10**, wherein said roughening step includes forming an adherent surface layer of a material selected from a group consisting of iridium oxide and titanium nitrate overlying said stent.

13. The method of claim **12**, including selecting said stent to have a sidewall thickness in a range from about 50 μm to about 75 μm after said surface layer is formed thereon.

14. A small profile stent delivery system adapted to traverse a vessel of less than 2.5 mm diameter in a human body, said stent delivery system including a catheter, a balloon having an inflated diameter less than about 2.5 mm at nominal pressure between about 6 and 8 atm integrated distally on said catheter for selective inflation and deflation through an inflation lumen of said catheter, a stent mounted on said balloon, said stent comprising an expandable diameter metal tube, the combination of said balloon when uninflated and said stent mounted thereon having a crossing profile in a range from approximately 0.5 mm to approximately 0.8 mm, said stent having a coating overlying an exposed surface thereof adapted to reside in contact with said balloon when said stent is mounted thereon, said coating including material to enhance fluoroscopic visibility of said stent and to create a rough region along said exposed surface to increase the retention force between said stent and said balloon.

15. The small profile stent delivery system of claim **14**, wherein said coating is devoid of adhesives.

16. The small profile stent delivery system of claim 14, wherein said coating comprises a ceramic-like material.

17. The small profile stent delivery system of claim 16, wherein said ceramic-like material is selected from a group consisting of iridium oxide and titanium oxide.

18. The small profile stent delivery system of claim 14, wherein said stent sidewall has a total thickness in a range from about 50 μm to about 75 μm.

* * * * *

US006071305A

United States Patent [19]

Brown et al.

[11] **Patent Number: 6,071,305**

[45] **Date of Patent: Jun. 6, 2000**

[54] **DIRECTIONAL DRUG DELIVERY STENT AND METHOD OF USE**

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[73] Assignee: **Alza Corporation**, Del.

[21] Appl. No.: **08/976,725**

[22] Filed: **Nov. 24, 1997**

Related U.S. Application Data

[60] Provisional application No. 60/031,471, Nov. 25, 1996.

[51] **Int. Cl.**[7] **A61F 2/06**

[52] **U.S. Cl.** **623/1**; 623/12; 606/198; 606/191

[58] **Field of Search** 623/1, 12; 604/891.1, 604/892.1; 606/198, 191

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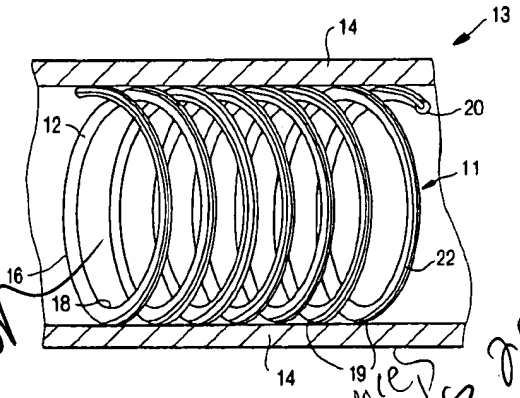
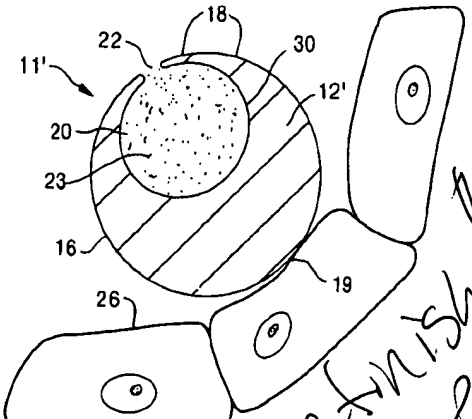
Primary Examiner—David H. Willse
Assistant Examiner—Suzette J. Jackson
Attorney, Agent, or Firm—Burns, Doane, Swecker & Mathis, L.L.P.

[57] **ABSTRACT**

The invention relates to a directional drug delivery stent which includes an elongated or tubular member having a cavity containing a biologically active agent. In one embodiment, the active agent is diffused from the reservoir directly to the walls of a body lumen, such as a blood vessel, through directional delivery openings arranged on an outer surface of the elongated member. Another variation of the stent includes an osmotic engine assembly for controlling the delivery of the active agent from the reservoir. The drugs which may be applied by the directional delivery stent include, but are not limited to, steroids, anti-inflammatory agents, restenosis preventing drugs, anti-thrombotic drugs, and tissue growth regulating drugs. The invention also relates to a method of using the directional drug delivery stent.

21 Claims, 8 Drawing Sheets





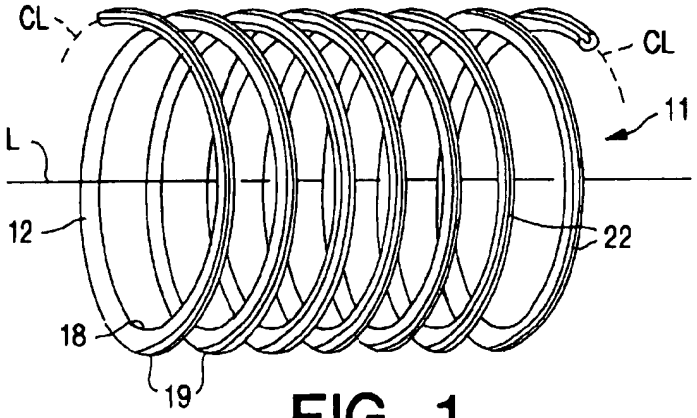


FIG. 1

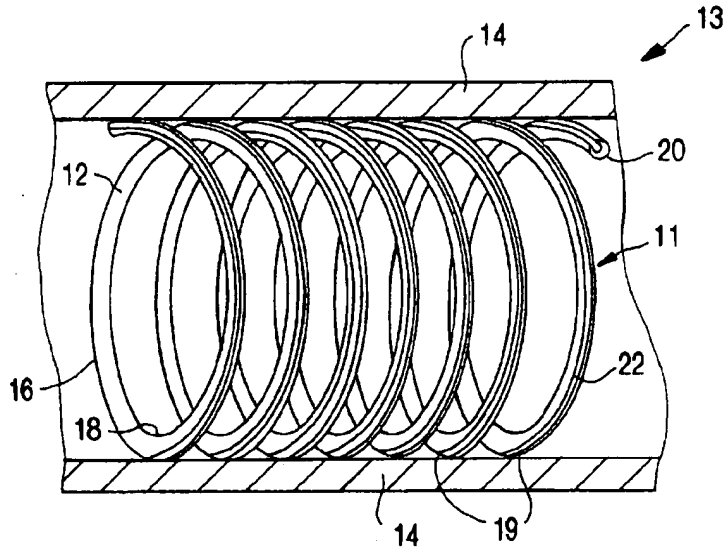


FIG. 2

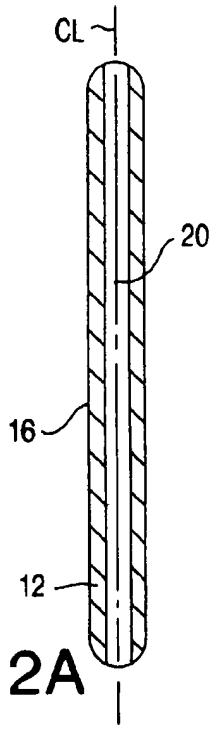


FIG. 2A

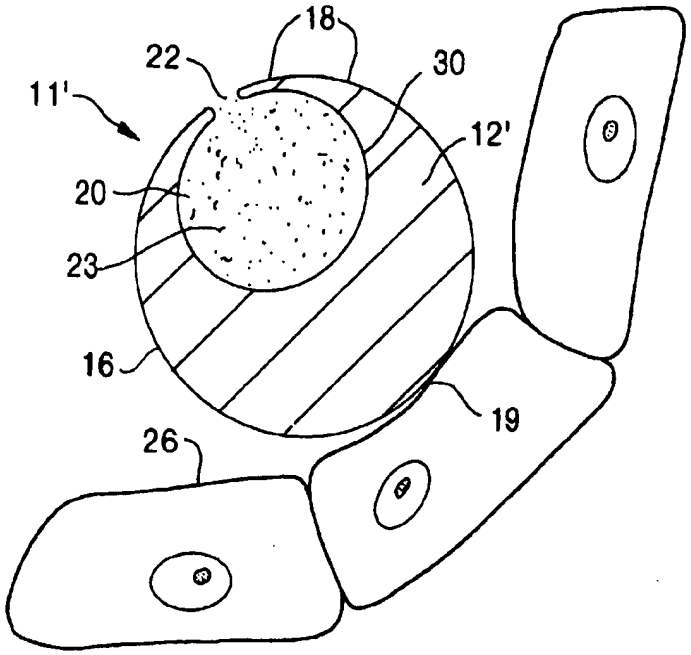


FIG. 3

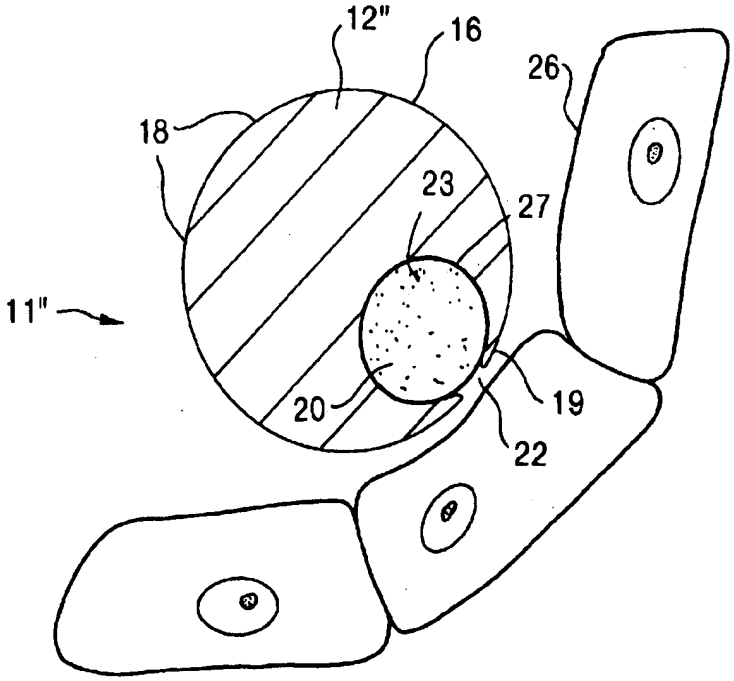


FIG. 4

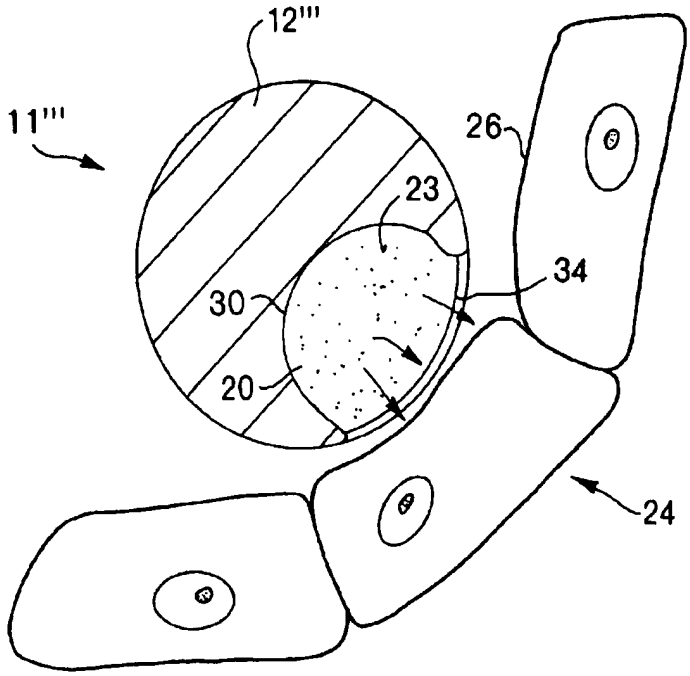


FIG. 5

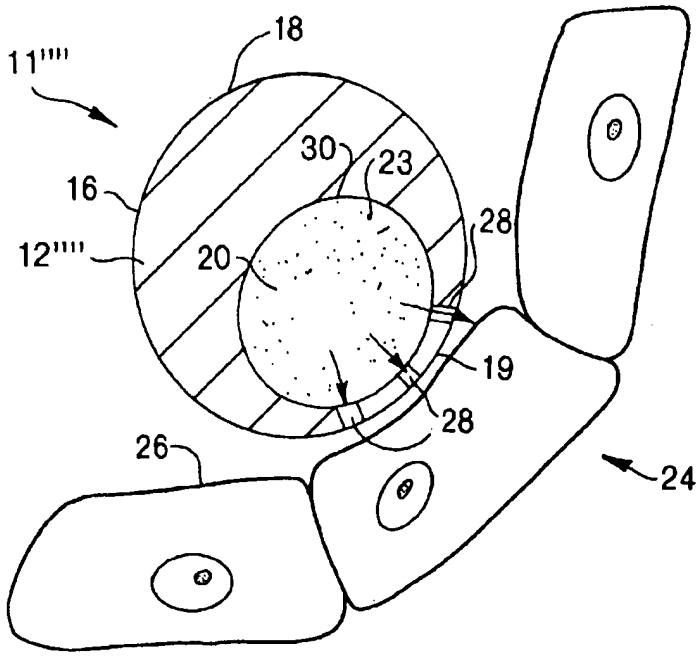


FIG. 6

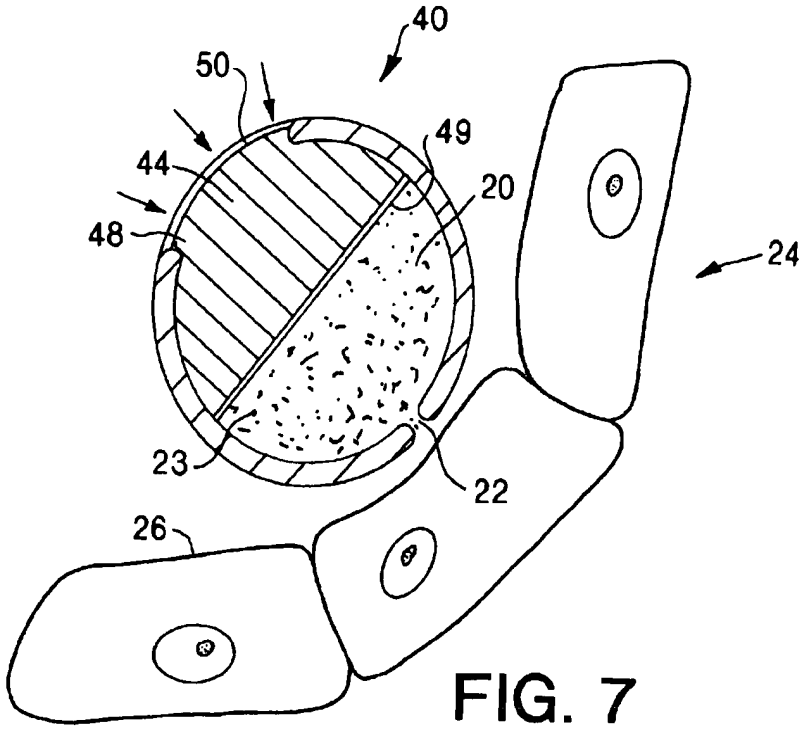


FIG. 7

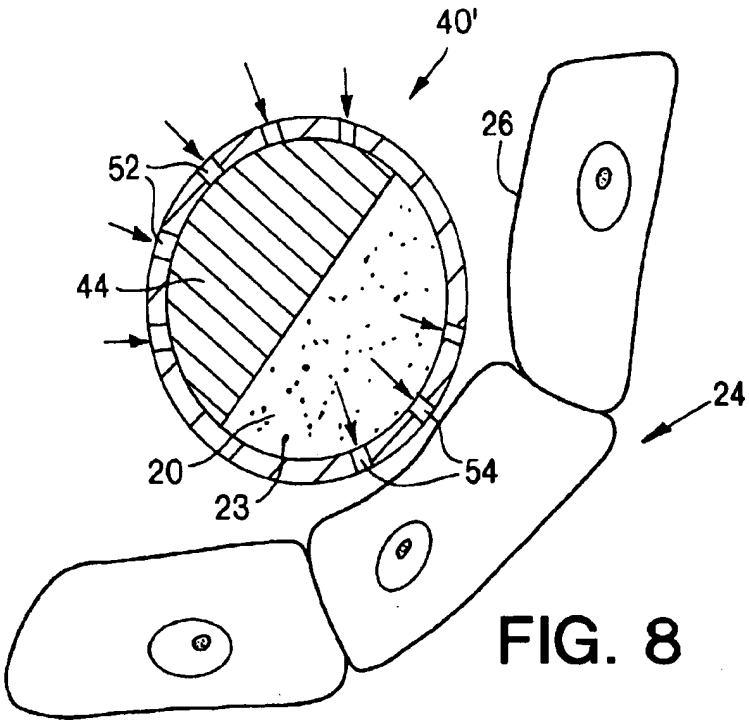


FIG. 8

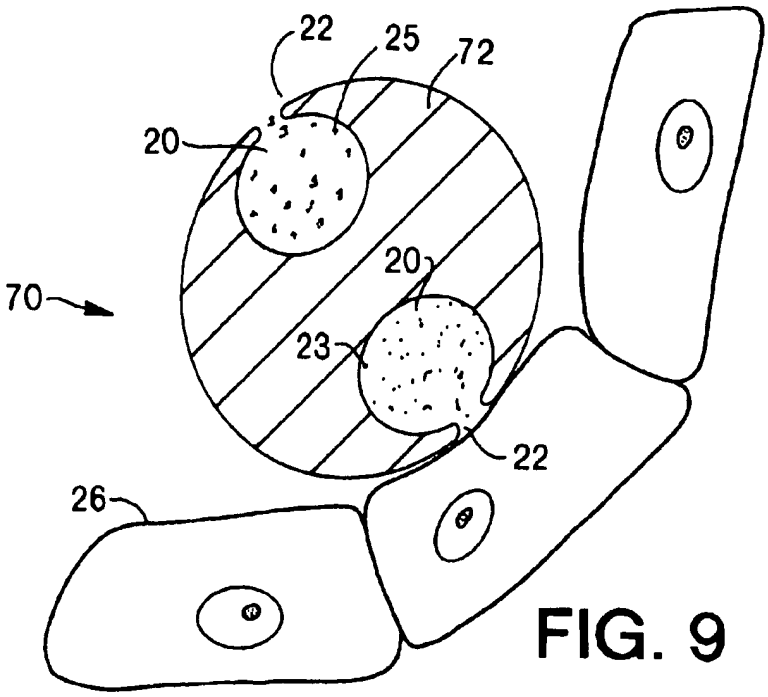


FIG. 9

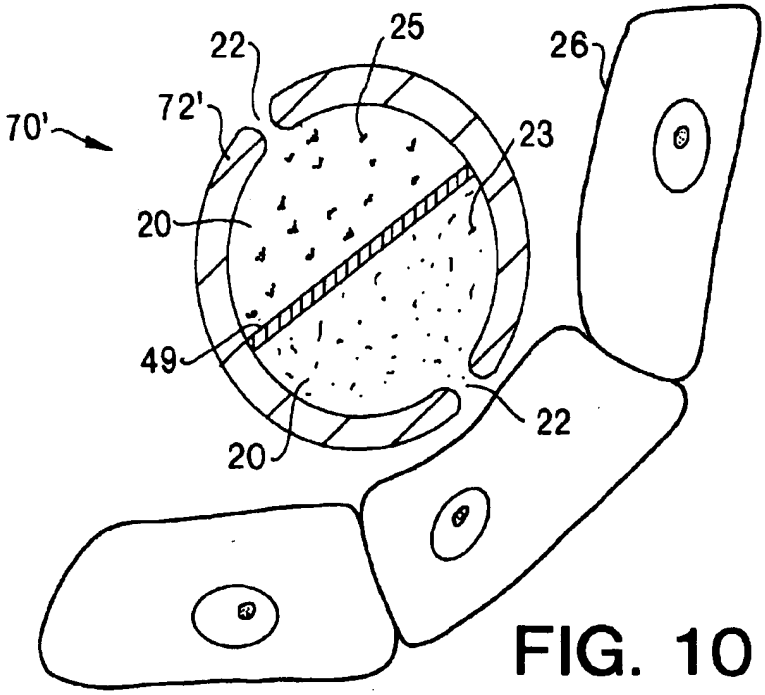


FIG. 10

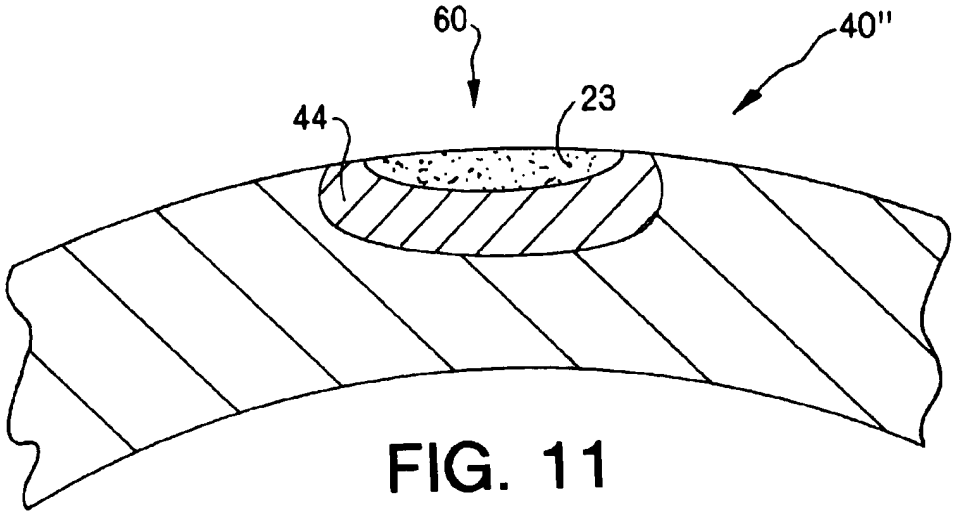


FIG. 11

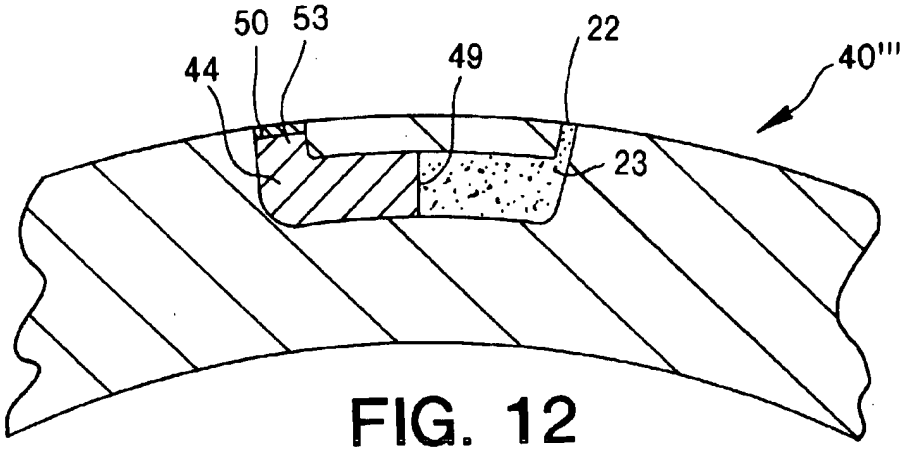


FIG. 12

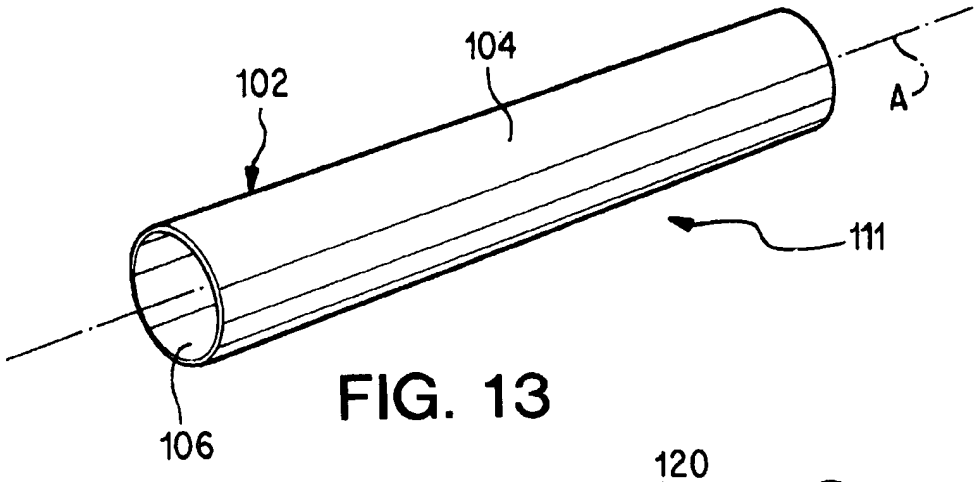


FIG. 13

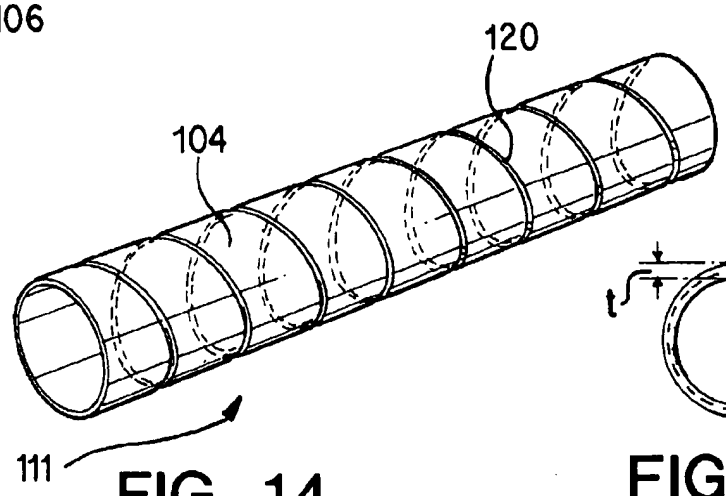


FIG. 14

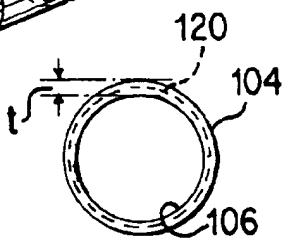


FIG. 14A

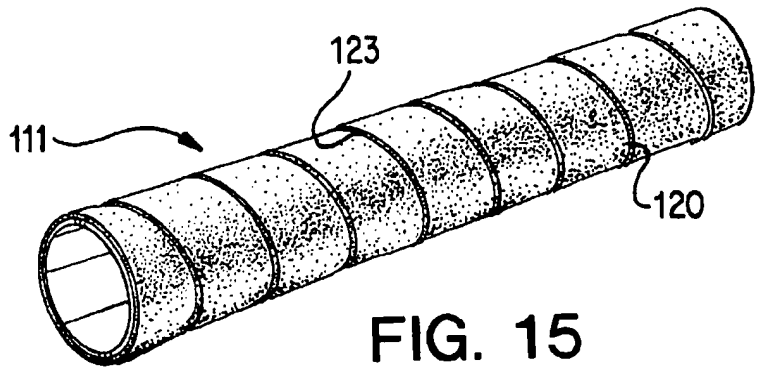


FIG. 15

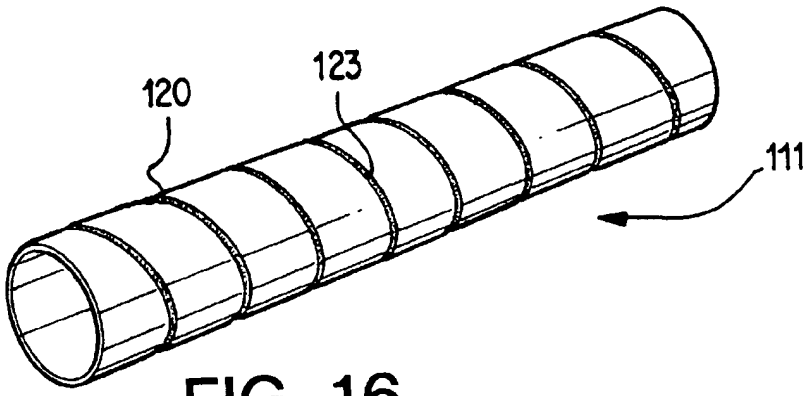


FIG. 16

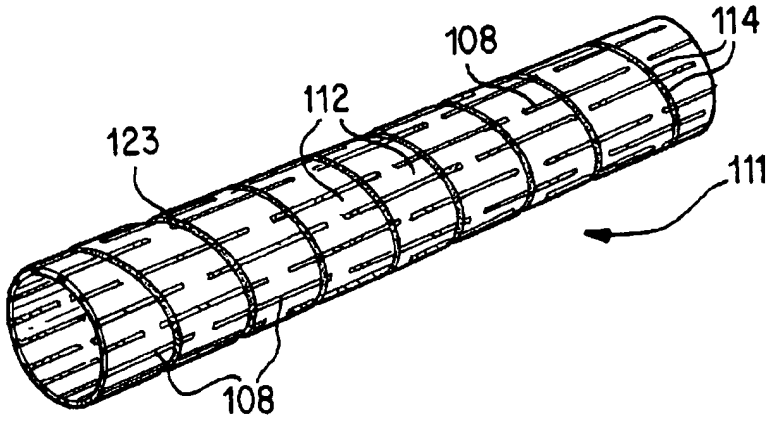


FIG. 17

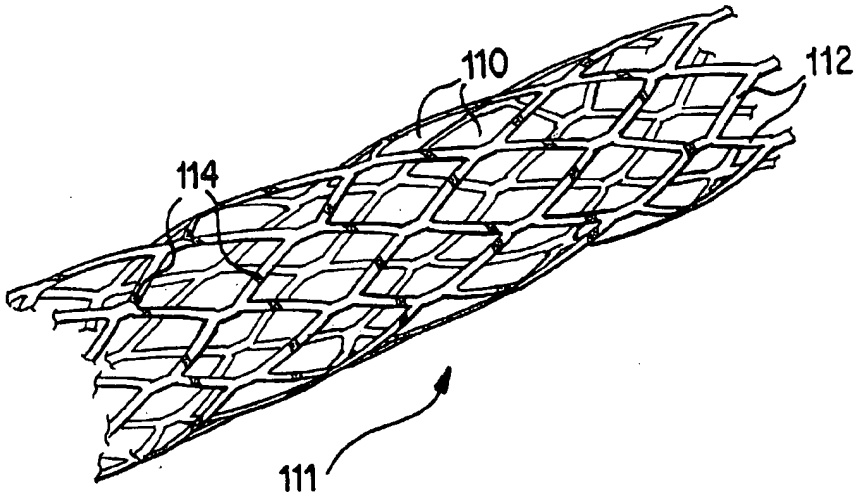


FIG. 18

DIRECTIONAL DRUG DELIVERY STENT AND METHOD OF USE

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 60/031,471, filed Nov. 25, 1996, pursuant to 35 U.S.C. § 119(e).

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a device and method for the directional delivery of a biologically active agent. More particularly, the invention relates to a stent made from an elongated member which has a cavity or interior containing an active agent for sustained directional delivery to a predetermined location in a body lumen, such as the wall of the body lumen.

2. Description of the Related Art

Many diseases cause body lumens to undergo stenosis or a narrowing of a canal within the body. Arteriosclerosis refers generally to a group of diseases in which the lumen of a blood vessel becomes narrowed or blocked, which may prevent a sufficient amount of blood from flowing through the blood vessel to the tissue. This shortage of blood flow caused by arteriosclerosis ultimately can permanently damage tissue and organs.

The therapeutic alternatives available for treatment of arteriosclerotic diseases include dilation of the artery using a pharmaceutical, surgical intervention to remove the blockage, replacement of the blocked segment with a new segment of artery, or the use of a catheter-mounted device such as a balloon catheter to dilate the artery. The dilation of an artery with a balloon catheter is called percutaneous transluminal angioplasty. During angioplasty, a balloon catheter in a deflated state is inserted within a stenotic segment of a blood vessel and is inflated and deflated a number of times to expand the vessel. Due to the inflation of the balloon catheter, the plaque formed on the vessel walls cracks and the vessel expands to allow increased blood flow through the vessel.

Often angioplasty permanently opens previously occluded blood vessels; however, restenosis, thrombosis, or vessel collapse may occur following angioplasty. Restenosis refers to the re-narrowing of an artery after an initially successful angioplasty due to exaggerated healing which causes a proliferation of tissue in the angioplasty area. Thrombosis is a clotting within a blood vessel which may cause infarction of tissues supplied by the blood vessel. In order to prevent restenosis and vessel collapse, stents of various configurations have been used to hold the lumen of a blood vessel open following angioplasty. However, stents do not entirely reduce the occurrence of thrombotic abrupt closure due to clotting; stents with rough surfaces exposed to blood flow may actually increase thrombosis, and restenosis may still occur because tissue may grow through and around the lattice of the stent. To prevent restenosis and thrombosis in the area where angioplasty has been performed, antithrombic agents and other biologically active agents can be employed.

Several stents exist which attempt to deliver active agents to the area in which angioplasty was performed. Some of these stents are biodegradable stents which have been impregnated with active agents. Examples of such impregnated stents are those disclosed in U.S. Pat. Nos. 5,500,013; 5,429,634; and 5,443,458. Other known agent delivery stents include a stent disclosed in U.S. Pat. No. 5,342,348 which includes a biologically active agent impregnated in delivery matrix filaments which may be woven into a stent or laminated onto a stent. U.S. Pat. No. 5,234,456 discloses a hydrophilic stent which can include a biologically active agent disposed within the hydrophilic material of the stent.

Other biologically active agent delivery stents are disclosed in U.S. Pat. Nos. 5,201,778; 5,282,823; 5,383,927; 5,383,928; 5,423,885; 5,441,515; 5,443,496; 5,449,382; 4,464,450; and European Patent Application No. 0 528 039. Other active agent delivery devices are disclosed in U.S. Pat. Nos. 3,797,485; 4,203,442; 4,309,776; 4,479,796; 5,002,661; 5,062,829; 5,180,366; 5,295,962; 5,304,121; 5,421,826; and International Application No. WO 94/18906.

Although known biologically active agent delivery stents deliver a biologically active agent to the area in which angioplasty was performed, they do not directionally deliver the active agent and, consequently, much of the biologically active agent is directed into the blood stream and does not reach the blood vessel wall where treatment is needed. Furthermore, these known agent delivery stents may actually increase the possibility of thrombosis. For example, some current stents attempt to reduce the risk of thrombosis by incorporating an extremely smooth and electropolished surface on the stent. However, this surface is ineffective against thrombosis when such stents are coated with a polymeric drug delivery system that is exposed to the bloodstream; the presence of such polymer drug delivery systems on current stents in the path of the bloodstream may actually initiate clotting.

The previously described problems associated with non-directional beneficial agent delivery provided by current agent delivery stents limits their range of effective use. Because of the above identified constraints of current delivery stents, it is very difficult to administer biologically active agents directionally to a desired area of a body lumen. As described above, delivering a biologically active agent to the walls of a blood vessel is problematic because non-directional delivery of the agent using current delivery stents results in much of the agent being carried away with the blood stream. The previously described constraints of current agent delivery stents has created a need for a solution.

SUMMARY OF THE INVENTION

The device according to the present invention addresses the disadvantages of the prior art by providing a directional delivery stent for delivering a biologically active agent. The stent according to the present invention includes a cavity or interior for containing the biologically active agent which is directionally delivered directly to a desired area of a body lumen, such as the wall of a blood vessel.

According to one aspect of the present invention, a biologically active agent delivery stent is nonbiodegradable and expandable for supporting a body lumen. The stent has an elongated member which has a center line extending along the elongated member. The center line of the elongated member is located radially spaced from the longitudinal center axis of the stent. At least one cavity is formed within the main body of the elongated member for containing at least one biologically active agent, and delivery means are located in only a portion of the circumference of the elongated member for directionally delivering the at least one biologically active agent from the cavity to an exterior of the elongated member.

According to another aspect of the present invention, the elongated member of the directional delivery stent includes

an outer surface having a luminal portion and a support portion. The support portion of the outer surface is for supporting a wall of the body lumen. The delivery means directionally delivers the biologically active agent from the cavity through only one of the luminal portion and the support portion.

According to another aspect of the present invention, the nonbiodegradable and expandable stent for supporting a body lumen has a longitudinal axis. The stent includes at least one tubular member having a center axis not coincident with the longitudinal axis of the stent. The tubular member has an interior for containing the at least one biologically active agent, and at least one fluid opening in only a portion of a circumference of the tubular member such that the biologically active agent may be delivered from the interior to a predetermined location.

According to another aspect of the present invention, the directional drug delivery stent includes an osmotic agent provided within the elongated or tubular member for osmotically delivering the biologically active agent.

According to a further aspect of the present invention, the biologically active agent is contained within a delivery matrix located within the cavity or interior.

According to a further aspect of the present invention, a method of directionally delivering a biologically active agent from a nonbiodegradable and expandable stent for supporting a body lumen and having a longitudinal axis, the stent including at least one tubular member having a center axis not coincident with a longitudinal axis of the stent, includes the steps of positioning the stent within a body lumen, and delivering the active agent from a cavity in a tubular member through at least one fluid opening in only a portion of a circumference of the tubular member such that the active agent is delivered to a predetermined location.

According to a further aspect of the present invention, a nonbiodegradable and expandable stent for directionally delivering an active agent includes a nonbiodegradable tubular member that has an exterior surface and an interior surface together defining a tubular member thickness of the tubular member. The tubular member has a recessed active agent receiving portion formed in the exterior surface. The recessed active agent receiving portion has a depth less than the tubular member thickness. The recessed active agent receiving portion contains at least one active agent.

According to a further aspect of the present invention, a method of manufacturing a nonbiodegradable stent includes the steps of: providing a nonbiodegradable tubular member having an exterior surface and an interior surface together defining a tubular member thickness of the tubular member; forming a recessed active agent receiving portion in the exterior surface of the tubular member, the recessed active agent receiving portion having a depth less than the tubular member thickness; and positioning an active agent in the recessed active agent receiving portion.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be described in greater detail with reference to the accompanying drawings in which like elements bear like reference numerals, and wherein:

FIG. **1** is a perspective view of a stent according to the present invention;

FIG. **2** is a cross sectional side view of a body lumen and a perspective view of a stent according to the present invention located therein.

FIG. **2A** is an enlarged sectional view of a portion of the stent of FIG. **2**.

FIG. **3** is an enlarged cross-sectional view of the elongated member of a stent according to the present invention positioned in a body lumen;

FIG. **4** is an enlarged cross-sectional view of the elongated member of an alternative embodiment of a stent according to the present invention positioned in a body lumen;

FIG. **5** is an enlarged cross-sectional view of the elongated member of an alternative embodiment of a stent according to the present invention positioned in a body lumen;

FIG. **6** is an enlarged cross-sectional view of the elongated member of an alternative embodiment of a stent according to the present invention positioned in a body lumen;

FIG. **7** is an enlarged cross-sectional view of the elongated member an osmotic directional delivery stent according to the present invention positioned in a body lumen; and

FIG. **8** is an enlarged cross-sectional view of the elongated member of an alternative embodiment of an osmotic directional delivery stent according to the present invention positioned in a body lumen;

FIG. **9** is an enlarged cross-sectional view of the elongated member of an alternative embodiment of a multi-directional delivery stent according to the present invention positioned in a body lumen;

FIG. **10** is an enlarged cross-sectional view of the elongated member of an alternative embodiment of a multi-directional delivery stent according to the present invention positioned in a body lumen;

FIG. **11** is an enlarged cross-sectional side view of the elongated member of an alternative embodiment of an osmotic directional delivery stent according to the present invention;

FIG. **12** is an enlarged cross-sectional side view of the elongated member of an alternative embodiment of an osmotic directional delivery stent according to the present invention;

FIG. **13** is perspective view of a tube that is a precursor of a stent according to an embodiment of the present invention;

FIG. **14** is a perspective view of a tube of FIG. **13** with a groove;

FIG. **14A** is an end view of the tube of FIG. **14**;

FIG. **15** is a perspective view of a grooved tube of FIGS. **14** and **14A**, where the grooved tube is coated with an active agent;

FIG. **16** is a perspective view of a grooved tube of FIG. **15**, where only the groove contains an active agent;

FIG. **17** is a perspective view of a grooved tube of FIG. **16** with a plurality of slots formed therein; and

FIG. **18** is a perspective view of an expanded stent according to an embodiment of the present invention obtained from the grooved tube of FIG. **17**.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

One aspect of the present invention relates to a directional drug delivery stent **11** including a cavity **20** containing a biologically active agent for directional application. For example, active agents may be directionally applied by diffusion to prevent restenosis, thrombosis, inflammation, to encourage healing, and/or to provide numerous other treatments.

The term "active agent" as used herein is intended to include one or more biologically active agents in combination with pharmaceutically acceptable carriers and, optionally, additional ingredients such as antioxidants, stabilizing agents, permeation enhancers, and the like.

The active agents which may be applied by the present invention generally belong to several basic groups including anti-inflammatory agents which prevent inflammation, restenosis preventing drugs which prevent tissue growth, antithrombogenic drugs which inhibit or control formation of thrombus or thrombolytics, and bioactive agents which regulate tissue growth and enhance healing of the tissue. Examples of active agents which may be used in the present invention include but are not limited to steroids, fibronectin, anti-clotting drugs, anti-platelet function drugs, drugs which prevent smooth muscle cell growth on inner surface wall of vessel, heparin, heparin fragments, aspirin, coumadin, tissue plasminogen activator (TPA), urokinase, hirudin, streptokinase, antiproliferatives (methotrexate, cisplatin, fluorouracil, Adriamycin), antioxidants (ascorbic acid, beta carotene, vitamin E), antimetabolites, thromboxane inhibitors, non-steroidal and steroidal anti-inflammatory drugs, beta and calcium channel blockers, genetic materials including DNA and RNA fragments, complete expression genes, antibodies, lymphokines, growth factors, prostaglandins, leukotrienes, laminin, elastin, collagen, and integrins.

The active agents may be anhydrous or aqueous solutions, suspensions or complexes with pharmaceutically acceptable vehicles, or carriers such that a biologically active amount of agent is delivered. Agent formulations that may be stored for long periods on the shelf or under refrigeration are preferred. The active agents may include pharmaceutically acceptable carriers and additional inert ingredients. In addition, more than one active agent may be incorporated into a formulation for delivery by the stent according to the present invention.

The directional drug delivery stent **11** according to one embodiment of the present invention illustrated in FIG. **1** is formed from an elongated or tubular member **12**. The embodiment of the directional drug delivery stent according to the present invention illustrated in FIGS. **1** and **2** is in the shape of a coil or helix, and is expanded within a body lumen by any known method such as by inflation of a balloon catheter or by heating of shape memory materials.

The tubular or elongated member **12** of the directional drug delivery stent **11** which is illustrated in FIGS. **1**, **2** and **2A** is formed with an interior or cavity **20**, which according to the embodiment of the present invention illustrated in FIGS. **2**, and **2A**, is a concave groove within the interior of the elongated member **12**, and extending along the entire length of the elongated member. Although the cavity **20** illustrated in FIG. **2** is a concave groove, the interior may be other configurations and need not extend the entire length of the elongated or tubular member **12**.

The elongated member **12** of the directional drug delivery stent according to the present invention illustrated in FIGS. **1** and **2** has a center line or center axis CL that runs along the length of the elongated member, such that it follows the path of the elongated member. Thus, if the elongated member **12**, which forms the directional drug delivery stent **11** of the embodiment of the present invention illustrated in FIGS. **1** and **2**, is in a coil shape, the center line or center axis CL of the elongated member also is in the shape of a coil.

The elongated member **12** of the present invention illustrated in FIGS. **1** and **2** is elongated, such as a strand, filament or fiber, and preferably has a cross section that is circular. However, the elongated member **12** may be other shapes. For example, the cross section of the elongated member taken along a plane perpendicular to the center line CL of the elongated member may be oval, elliptical, octagonal or square, for example.

The elongated member **12** of the illustrated directional drug delivery stent **11** also has a fluid opening or delivery means for directionally delivering a biologically active agent within the cavity or interior **20**. As illustrated in FIGS. **1** and **2**, the fluid opening or delivery means may be a slit shaped opening **22** extending along the outer surface **16** of the stent which allows the active agent to be delivered from the cavity **20**. Although the slit shaped opening **22** is illustrated, any number of fluid opening configurations may be fashioned. For example, a series or plurality of holes, grooves, small indentations, and intermittent recessions could all be fluid openings and delivery means for directionally delivering the biologically active agent. Furthermore, the opening **22** need not extend the entire length of the elongated member **12**. For example, the delivery means **22** may be located intermittently along the length of the tubular member **12**.

As illustrated in FIG. **2**, the stent **11**, according to one embodiment of the present invention, may be positioned in a body lumen **13**, such as a blood vessel, bronchial passageway, intestine, the rumen of an animal, nasal cavity, cervical area, or ear, for example. The drug delivery stent **11** illustrated in FIGS. **1** and **2** has an outer surface **16** having a luminal portion **18** for contacting the interior of the body lumen, which may include a luminal fluid, bodily liquid, gas, air, or any other substance that may be within the body lumen. The outer surface **16** also has a support portion **19** for supporting the walls **14** of the body lumen **13**, which may be an exemplary blood vessel. The location of the slit shaped opening **22** along the outer surface **16** of the stent **11** provides directional drug delivery of the active agent from the cavity or interior **20**. For example, in the embodiment of the present invention illustrated in FIG. **2**, the delivery means, fluid opening, or exemplary slit **22** is positioned such that the active agent is delivered directly to the wall **14** of the body lumen **13**. Because the slit **22** of the embodiment of the present invention illustrated in FIG. **2** directionally delivers the biologically active agent from the cavity **20** only through the support portion **19**, the active agent is not directed into the interior of the body lumen, but is instead delivered to the walls **14**. Thus, the fluid opening, or slit opening **22** in FIGS. **1** and **2** is only in a portion of the circumference of the outer surface **16** of the tubular member **12**, permitting the biologically active agent **23** in the interior or cavity **20** to be directionally delivered exteriorly of the elongated member at a predetermined location, which in the embodiment illustrated in FIG. **2**, is the wall **14**. This is particularly advantageous when the drug delivery stent illustrated in FIG. **2** is used in a blood vessel; because the slit opening **22** of the embodiment of the present invention illustrated in FIG. **2** is located at the support portion **19**, the blood stream of a blood vessel is only exposed to the smooth and luminal portion **18** of the stent **11**, minimizing the possibility of thrombosis after the stent is expanded within the blood vessel.

Although the directional drug delivery stent **11** illustrated in FIG. **2** includes a fluid opening **22** located at the support portion **19** of the elongated member **12** such that the wall **14** immediately adjacent the fluid opening is the predetermined location where directional drug delivery occurs, other predetermined locations are possible. Generally speaking, the delivery means or fluid opening **22** is only in a portion of the circumference of the elongated or tubular member **12**; the circumference is the perimeter, periphery or boundary line

of the cross sectional area of the elongated or tubular member taken along the plane perpendicular to the center line CL of the elongated member. Thus, because the delivery means is only in a portion of the circumference of the elongated member, the biologically active agent located within the cavity or interior **20** is delivered exteriorly of the elongated member through the delivery means or fluid opening at a predetermined location. Directionally delivery occurs over less than the entire circumferential extent such that the biologically active agent is delivered to a predetermined location.

The elongated member **12** is preferably formed of a fairly rigid, impermeable, and strong material which is non-biodegradable. The elongated member material is preferably a biocompatible metal or alloy such as stainless steel, titanium, platinum, tantalum, silver, tungsten, gold, and their alloys as well as gold-plated ferrous alloys, platinum-plated ferrous alloys, cobalt-chromium alloys and titanium nitride coated stainless steel. Alternatively, the elongated or tubular member **12** may be formed of a polymer, such as polyether sulfone, polyamide, polycarbonate, polypropylene, high molecular weight polyethylene, carbon fiber, and the like. The elongated member **12** may also be formed of semipermeable or micro-porous material.

The helical stent **11** according to one embodiment of the present invention used in blood vessels has an initial diameter at which it is inserted into a body lumen, and an expanded final diameter. For many such applications, the initial diameter of the stent **11** will be in the range of from about 1.25 mm to 2 mm and the expanded final diameter will be from about 2 mm to about 6 mm. The stent **11** desirably has the property such that it retains its shape after expansion by a balloon catheter or other method.

Although the stent **11** formed from the elongated member **12** illustrated in FIG. **1** has a helical or coil shape, the present invention relates to stents having other configurations such as coiling stents, expandable tube stents, roving wire stents, and wire mesh stents. Thus, the elongated member **12** may be the filaments or fibers which form a mesh stent. In such alternative stent configuration, the directional drug delivery stent according to the present invention, like the stent **11** illustrated in FIGS. **1** and **2**, will have a longitudinal axis or longitudinal center axis L, which is, generally, an imaginary substantially straight line running the longer direction of the stent and about which the body of the stent is symmetrically arranged. The center axis or the center line CL of the tubular or elongated member **12** of the directional drug delivery stent according to the present invention will not be coincident with the longitudinal axis or the longitudinal center axis L of the stent. In other words, the center line CL of the elongated member **12** is located radially spaced from the longitudinal center axis L of the stent **11**.

The tubular member **12** of the stent **11** is formed of a material which is not biodegradable, bioerodible, or resorbable and remains in the body lumen to prevent collapse of the body lumen walls even after the active agent **23** has been completely diffused from the cavity. The stent **11** functions both to physically support the body lumen wall and also to prevent restenosis and thrombosis by directionally delivering the active agent **23** to a predetermined location, such as a body lumen wall or a luminal fluid. Thus, the stent **11** according to one embodiment of the present invention prevents restenosis, thrombosis, and collapse of the blood vessel more completely than the prior art stents which do not provide both physical support of the blood vessel without exposure to a thrombogenic surface, and delivery of an active agent directly to the vessel walls. Furthermore, by delivering the active agent directly to the vessel walls, more efficient use of the active agent is possible and there is no exposure of thrombogenic polymers or agents to the blood vessel.

An enlarged cross-sectional view of the elongated member **12'** of the stent **11'**, according to one embodiment of the present invention positioned in a body lumen is illustrated in FIG. **3**. As shown in FIG. **3**, the elongated member **12'** of the stent **11'** has an interior or cavity **20**, which in the illustrated embodiment is a concave shaped groove. The cavity **20** illustrated in FIG. **2** is formed by the surface **30**. In the case of a helical stent **11'**, the cavity **20** and the slit shaped opening **22** extend along the helical path of the elongated member **12'**. In the embodiment of the present invention illustrated in FIG. **3**, the depth of the cavity **20** within the stent **11'** is no more than half the cross section diameter of the elongated member **12'**, although any depth may be used which still allows the stent **11'** to structurally support the lumen walls.

The cavity **20** of the embodiment of the present invention illustrated in FIG. **3** has an elongated or oval cross-sectional shape with the elongated side of the oval at the outer surface **16** of the tubular member **12'**. However, the size and shape of the interior or cavity **20** can be any number of shapes and still be within the confines of the present invention. Furthermore, the size and shape of the cavity **20** may be varied to control the total amount of active agent **23** which is delivered and the rate of delivery. The size of the delivery means or fluid opening, which is a slit shaped opening **22** in the embodiment of the present invention illustrated in FIG. **3** can also be varied to control the rate of delivery of the active agent **23**. The width of the slit shaped opening **22** of the embodiment of the present invention illustrated in FIGS. **1**, **2** and **3** is between 0.1 and 49%, preferably between 10 and 25%, of the circumference of the elongated member **12** and **12'**.

The embodiment of the present invention illustrated in FIG. **3** directionally delivers the biologically active agent **23** into the interior of the body lumen, which may include a fluid, gas, or other bodily substance. The delivery means, or the slit opening **22** has a width as described above, and permits directional delivery of the biologically active agent **23** from the cavity **20** through only the luminal portion **18** of the outer surface **16** of the elongated member **12'**. The biologically active agent **23** is not directionally delivered to the wall **26** of the body lumen in the embodiment of the present invention illustrated in FIG. **3**. Thus, the present invention permits directional delivery to a predetermined location, which in FIG. **3** is the interior of the body lumen or a luminal fluid located therein, by providing at least one fluid opening in only a portion of the circumference of the tubular member.

FIG. **4**, like FIG. **2**, illustrates a stent **11"** according to another embodiment of the present invention which directionally delivers the biologically active agent **23** from the cavity **20** and through the slit opening **22**, which is located at the support portion **19** of the outer surface **16**, such that the biologically active agent is delivered to the body lumen wall **26**.

As illustrated in the embodiment of the present invention shown in FIG. **4**, the cavity **20** preferably contains a biocompatible delivery matrix **27** containing a biologically active agent for release. Such an exemplary delivery matrix **27** may be a biodegradable or non-biodegradable material. Examples of biocompatible polymeric matrix **27** formulations which may be disposed within the cavity **20** and

incorporate the active agents **23** are polymers such as poly-ethylene-vinyl acetate, polyethylene, polyesters, poly anhydrides, polyorthoesters, polyamides, polyethers, and polyurethanes. Other delivery matrix **27** compounds such as waxes, fats or other biocompatible materials may also hold the biologically active agents **23**. However, as illustrated in FIG. **3**, no delivery matrix **27** is needed, especially if the biologically agent **23** has a sufficiently low solubility, permitting controlled diffusional delivery of the agent.

As depicted in FIG. **5**, the elongated member **12'''** of the stent **11'''**, according to another embodiment of the present invention may also optionally include delivery means having a membrane **34** which covers the slit shaped opening and allows the active agent to diffuse through the membrane to the desired predetermined location. The membrane **34** may be selected to provide a desired diffusional delivery rate of the active agent **23**. Suitable membranes **34** for use in the present invention to control the delivery of the active agent **23** include, but are not limited to, poly-ethylene-vinyl acetate, polyethylene, polyesters, polyanhydrides, polyorthoesters, polyamides, polyethers, and polyurethanes.

According to an alternative embodiment of the present invention which is illustrated in FIG. **6**, the tubular member **12''''** of the stent **11''''**, is provided with a plurality of fluid openings or holes **28** in only a portion of the circumference of the elongated member which are the delivery means for directionally delivering the biologically active agent **23**. Directional delivery of the active agent is provided from the cavity **20** through the plurality of holes **28** to the lumen walls **26**. The size and number of the holes **28** may be varied to control the rate of delivery of the active agent from the stent **11''''**. The holes **28** occupy between 0.1 and 49%, preferably between 10 and 25% of the circumference of the tubular or elongated member **12''''**.

A further aspect of the present invention relates to an osmotic directional delivery stent **40** illustrated in FIG. **7**. According to the osmotic delivery version, the tubular member of the stent **40** includes an interior or cavity **20** having a biologically active agent **23** as in the embodiment of FIGS. **3–6**. However, the stent **40** also includes a fluid-imbibing osmotic agent **44** which is adjacent the biologically active agent **23**.

As shown in FIG. **7**, the tubular member of the stent **40** is provided with a fluid inlet opening **48** which allows fluid from, for example, the interior of the body lumen **24** to enter the osmotic agent **44** causing it to swell. The osmotic agent **44** may be an osmagent, an osmopolymer, or a mixture of the two. Species which fall within the category of osmagent, i.e., the non-volatile species which are soluble in water and create the osmotic gradient driving the osmotic inflow of water, vary widely. Examples are well known in the art and include magnesium sulfate, magnesium chloride, potassium sulfate, sodium chloride, sodium sulfate, lithium sulfate, sodium phosphate, potassium phosphate, d-mannitol, sorbitol, inositol, urea, magnesium succinate, tartaric acid, raffinose, and various monosaccharides, oligosaccharides and polysaccharides such as sucrose, glucose, lactose, fructose, and dextran, as well as mixtures of any of these various species. Species which fall within the category of osmopolymer are hydrophilic polymers that swell upon contact with water, and these vary widely as well. Osmopolymers may be of plant or animal origin, or synthetic, and examples of osmopolymers are well known in the art. Examples include: poly(hydroxy-alkyl methacrylates) with molecular weight of 30,000 to 5,000,000, poly(vinylpyrrolidone) with molecular weight of 10,000 to 360,000, anionic and cationic hydrogels, polyelectrolyte complexes, poly(vinyl alcohol) having low acetate residual, optionally cross linked with glyoxal, formaldehyde or glutaraldehyde and having a degree of polymerization of 200 to 30,000, a mixture of methyl cellulose, cross linked agar and carboxymethyl cellulose, a mixture of hydroxypropyl methycellulose and sodium carboxymethylcellulose, polymers of N-vinyllactams, polyoxyethylene-polyoxypropylene gels, polyoxybutylene-polyethylene block copolymer gels, carob gum, polyacrylic gels, polyester gels, polyuria gels, polyether gels, polyamide gels, polypeptide gels, polyamino acid gels, polycellulosic gels, carbopol acidic carboxy polymers having molecular weights of 250,000 to 4,000,000, Cyanamer polyacrylamides, cross linked indene-maleic anhydride polymers, Good-Rite polyacrylic acids having molecular weights of 80,000 to 200,000, Polyox polyethylene oxide polymers having molecular weights of 100,000 to 5,000,000, starch graft copolymers, and Aqua-Keeps acrylate polymer polysaccharides, inorganic salts, organic salts, sugars, polysaccharides, polymeric hydrogels, or amphoteric molecules.

The osmotic agent **44** operates by imbibing fluid from the biological environment of use **24** and causes the osmotic agent to expand in a controlled manner. The expanding osmotic agent **44** compresses the active agent **23** within the cavity **20** causing the active agent to be released in a controlled manner through the slit shaped opening **22** to a predetermined location, which in the embodiment illustrated in FIG. **7** is the wall **26** of the luminal body **24**. The fluid inlet opening **48** may also be located at the wall of the vessel, while the slit shaped opening **22** may be directed at the interior of the luminal body.

The size of the fluid inlet opening **48** may be varied to regulate the delivery rate of the active agent **23** by controlling the rate at which the fluid enters and swells the osmotic agent **44**. If the stent **40** is made of a semipermeable micro-porous material, no fluid inlet opening **48** is needed. The fluid inlet opening **48** to the cavity **20** may also be covered with a membrane **50** which controls the rate of delivery of the active agent by controlling the rate at which fluid from the body lumen **24** enters the osmotic agent **44**.

The embodiment of the present invention illustrated in FIG. **7** also includes an optional separating member **49** between the osmotic agent **44** and the biologically active agent **23**. The optional separating member **49** keeps the osmotic agent **44** separate from the biologically active agent **23** while also allowing the osmotic agent to swell. The separating member **49** may move within the cavity or interior **20**, or the separating member may be fixed within the cavity and made of a flexible material that stretches as the osmotic agent imbibes fluid from the biological environment of use. However, the separating member **49** is not required, and there may be only an interface between the osmotic agent **44** and the biologically active agent **23**.

FIG. **8** illustrates an alternative embodiment of the osmotic delivery stent **40'** in which a plurality of fluid inlet openings **52** are provided in the tubular member for allowing fluid to enter and swell the osmotic agent **44** in the cavity **20**. A plurality of holes **54** located in only a portion of the circumference of the tubular member are the delivery means or fluid openings for directionally delivering the active agent **23** from the cavity **20** to the wall **26** of the body lumen **24**. The number and size of the openings **52**, **54** may be varied to regulate the delivery rate of the active agent **23**.

FIG. **9** illustrates an alternative embodiment of a multi-directional delivery stent **70** according to the present inven-

tion in which the elongated or tubular member **72** includes two cavities or interiors **20**. Each of the two cavities contains a biologically active agent **23, 25** for directional delivery to two different predetermined locations. In this embodiment, the first biologically active agent **23** is directionally delivered to the wall **26** through the slit shaped opening **22** located in only a portion of the circumference of the elongated member, while the second biologically active agent **25** is located in the other of the two cavities **20** and is also directionally delivered to a predetermined location, which in this embodiment, is the interior of the body lumen. The first and second biologically active agents **23, 25** may be the same agent or different agents for different treatments.

FIG. **10** illustrates an alternative embodiment of the multi-directional delivery stent **70'** according to the present invention in which the elongated or tubular member **72'** includes one cavity **20** for containing a first biologically active agent **23** and a second biologically active agent **25**. The cavity **20** of the tubular member **12** includes a separating member **49** located between the biologically active agents **23, 25**. The separating member **49** may be a structural support maintaining the structural integrity of the elongated member **72'**, and/or a device, such as one of the above described membranes, for separating the two agents **23, 25** from each other within the cavity **20**. However, the separating member **49** is not required, leaving only an interface between the two agents **23, 25**; in such an embodiment, to maintain structural integrity of the tubular member **12** and stent **70'**, the slit shaped openings **22** would not run the entire length of the elongated member. Thus, the embodiment of the present invention illustrated in FIG. **10** includes two means or openings **22** located in only a portion of the circumference of the tubular member for delivering two biologically active agents **23, 25** from one cavity **20** to two different predetermined locations.

FIG. **11** illustrates a longitudinal cross sectional view of another alternative embodiment of an osmotic delivery stent **40"** according to the present invention. The stent **40"** includes an osmotic engine assembly **60**. The osmotic engine assembly **60** may be fashioned separately in the shape of a tablet or capsule and inserted into the interior or cavity of the stent **40"**. The osmotic engine assembly **60** includes the osmotic engine **44** and the biologically active agent **23**. The osmotic agent and/or the biologically active agent **23** may be optionally coated with a semipermeable membrane. Once the assembly **60** is positioned within the cavity, the oval shaped opening through which the osmotic engine **60** was inserted, permits both the fluid from the biological environment of use to enter the osmotic agent **44** and the biologically active agent **23** to exit the stent at the predetermined location.

FIG. **12** illustrates a longitudinal cross sectional view of another alternative embodiment of an osmotic delivery stent **40'"** according to the present invention. The stent **40'"** includes delivery means or fluid opening **22** through which the biologically active agent **23** is directionally delivered. The interior or cavity is shaped like a channel within the stent body and holds an osmotic agent **44** adjacent to the biologically active agent **23**. This embodiment of the present invention may optionally include a separating member **49** between the osmotic agent **44** and the biologically active agent **23**, and a semipermeable membrane **50** located at the fluid inlet opening **53**.

FIG. **17** illustrates an example of the aforementioned expandable tube-type stent **111** according to another embodiment of the present invention. FIG. **18** illustrates the stent **11** in an expanded state. FIGS. **13–17** illustrate one preferred method of making the stent **111**.

The expanded tube-type stent **111** is manufactured by cutting an elongated tubular member into tubular sections, one of which is shown in FIG. **13**. The tubular member may be manufactured from any of the nonbiodegradable materials described above in reference to the other embodiments of stents according to the present invention. For example, the tubular member may be made from titanium, stainless steel, nitinol, tantalum, or other similar materials. Although other configurations of the tubular member are contemplated, as FIG. **13** illustrates, the section of tubular member is preferably a cylindrical tube **102** having a longitudinal center axis A coincident with the longitudinal center axis of the finished stent **111**.

A recessed active agent receiving portion or groove **120** is formed in the exterior surface **104** of the tube **102**. The groove **120**, illustrated in FIG. **14**, is preferably a continuous helical or coiling groove extending around the tube **102**, although other configurations are contemplated such as straight, parallel, and zig-zagging grooves. In addition, the groove **120** need not be continuous. For example, a plurality of spaced apart grooves may be formed in the exterior surface **104** of the tube **102**. The groove **120** may be formed by methods well known in the art, but is preferably formed with a laser to define a groove having a concave shape when viewed in cross-section. As shown in FIG. **14A**, the groove **120** does not extend through the wall thickness t of the tube **102**. In other words, the groove **120** does not completely pierce through the interior surface **106** of the tube **102**, and so the depth of the groove is less than the wall thickness t (i.e., the tubular member thickness measured between the exterior surface **104** and the interior surface **106**). Similar to the previously described embodiments, the recessed active agent receiving portion or groove **120** defines a fluid opening through which an active agent **123** may be directionally delivered.

After the groove **120** has been formed in the exterior surface **104** of the tube **102**, the tube is coated with an active agent **123**, such as those described above. The active agent **123** may be applied to the exterior surface **104** by spraying the tube **102**, dipping the tube, or by other conventional methods. Because at least the entire exterior of the tube is coated, the groove **120** is also filled with the active agent **123**. In the embodiment illustrated in FIG. **15**, the exterior surface **104** is covered and the helical groove **120** is filled with a biocompatible delivery matrix containing a biologically active agent for release, similar to the stent **11"** illustrated in FIG. **4**.

After the tube **120** is coated with the active agent **123**, the excess biological active agent is preferably removed from the exterior surface of the tube **102**. As shown in FIG. **16**, this step of the manufacturing process of the stent **111** removes all active agent from the tube **102** except for the active agent in the groove **120**. The excess active agent may be removed, for example, by wiping the tube **102**, passing the tube through a tight fitting sleeve or collar, or scraping the tube. As a result of this step, the active agent **123** is only contained in the groove **120**. Alternatively, the active agent **123** may be left on the exterior surface **104** of the tube **102**, or the groove **120** may be directly filled with the active agent **123** without coating the entire exterior surface of the tube.

Once the recessed active agent receiving portion or groove **120** has been filled with active agent **123** such that it contains the active agent, a plurality of perforations, slits, or slots **108** are formed in the tube **102**, as illustrated in FIG. **17**. The slots **108** are formed in the exterior surface **104** of the tube **102**, and extend completely through the tubular member thickness or wall thickness t. The slots **108** are

preferably formed with a laser or other conventional apparatus. The through slots **108** shown in FIG. **17** are parallel and staggered, but may be any conventional configuration, so long as they permit the stent **111** to be expanded. For example, the slot **108** may extend straight along the entire length of the tube **102** such that the stent is split and coils upon itself like a wood shaving, or may helically extend around the tube such that the stent is shaped like a coil spring. Thus, it is apparent that at least one function of the slots is to permit the stent **111** to be expanded, such as illustrated in FIG. **18**, although, as described above in regard to other embodiments of the present invention, such slots may not be necessary for the stent to be expandable.

Because the preferred slots **108** extend longitudinally along the tube **102** and the preferred recessed active agent receiving portion or groove **120** extends helically around the tubular member, the slots intersect the groove to define a plurality of spaced apart groove portions **114**, each containing the active agent **123**. The spaced apart groove portions **114** are positioned relative to one another such that together they define or outline a helical shape, as shown in FIG. **17**.

Once the slots **108** have been formed in the tube **102**, it is apparent that the tube is expandable as shown in FIG. **18**. When the tube is expanded, the tubular material between the slots **108** forms the angled fibers or elongated members **112**, and the slots **108** form the interstitial openings **110**. Thus, as shown in FIG. **17**, the slots **108** in the unexpanded stent **111** define a plurality of parallel elongated members **112**. At least some of the elongated members **112** contain groove portions **114** or cavities in which the active agent is located. Hence, those portions of the elongated members **112** that contain groove portions **114** have an active agent delivery opening in only a portion of the circumference of the elongated member for directional delivery of the active agent **123** contained in the groove portion, similar to the previously described embodiments of the present invention. Because the slots **108** are formed with a laser, the elongated portions **112** tend to have a square or rectangular cross-sectional shape. Other conventional slot forming processes may form other cross sectional shapes of the elongated members **112**. As is apparent from FIGS. **17** and **18**, the individual fibers or elongated members **112** each have a longitudinal axis or center line that is located radially spaced from the longitudinal center axis of the stent **111**.

Like the previously described embodiments of stents according to the present invention, the tube **102** of the stent **111** is formed of a material which is not biodegradable, bioerodible, or resorbable and remains in the body lumen to prevent collapse of the body lumen walls even after the active agent **123** has been completely diffused from the cavity. The stent **111** functions both to physically support the body lumen wall and also to prevent restenosis and thrombosis by directionally delivering the active agent **123** to a predetermined location, such as a body lumen wall or a luminal fluid. Thus, the stent **111** can prevents restenosis, thrombosis, and collapse of the blood vessel more completely than the prior art stents which do not provide both physical support of the blood vessel without exposure to a thrombogenic surface, and delivery of an active agent directly to the vessel walls. Furthermore, by delivering the active agent **123** directly to the vessel walls, more efficient use of the active agent is possible and there is no exposure of thrombogenic polymers or agents to the blood vessel.

While the invention has been described in detail with reference to preferred embodiments thereof, it will be apparent to one skilled in the art that various changes can be made, and equivalents employed without departing from the spirit and scope of the invention.

We claim:

1. A nonbiodegradable and expandable stent for directionally delivering an active agent, the stent comprising:

a nonbiodegradable tubular member having an exterior surface and an interior surface together defining a tubular member thickness of said tubular member, said tubular member having a recessed active agent receiving portion formed in said exterior surface, said recessed active agent receiving portion having a depth less than said tubular member thickness, said recessed active agent receiving portion containing at least one active agent.

2. The stent according to claim **1**, wherein said recessed active agent receiving portion is a helical groove extending around said tubular member.

3. The stent according to claim **1**, further comprising a plurality of slots extending through said tubular member thickness, said recessed active agent receiving portion including a plurality of spaced apart groove portions, adjacent ones of said groove portions being separated by one of said slots.

4. The stent according to claim **3**, wherein when said stent is expanded said slots expand to increase a distance between adjacent ones of groove portions.

5. The stent according to claim **1**, wherein said tubular member is cylindrical.

6. The stent according to claim **1**, wherein said active agent is contained in a delivery matrix.

7. An expandable stent for directionally delivering an active agent, the stent comprising:

a nonbiodegradable and tubular member having an exterior surface and an interior surface together defining a tubular member thickness of said tubular member, said tubular member having a groove formed in said exterior surface, said groove having a depth less than said tubular member thickness, said groove containing at least one active agent.

8. The stent according to claim **7**, wherein said groove is helical.

9. The stent according to claim **7**, further comprising a plurality of slots extending through said tubular member thickness, said groove including a plurality of spaced apart groove portions, adjacent ones of said groove portions being separated by one of said slots.

10. The stent according to claim **9**, wherein said slots extend parallel with a longitudinal axis of said tubular member.

11. The stent according to claim **9**, wherein said slots are formed with a laser.

12. The stent according to claim **7**, wherein said active agent is contained in a delivery matrix.

13. The stent according to claim **7**, wherein said tubular member is pipe-shaped.

14. The stent according to claim **7**, wherein said active agent is one of steroids, anti-inflammatory agents, restenosis preventing drugs, anti-thrombotic drugs, and tissue growth regulating drugs.

15. The stent according to claim **7**, wherein said groove is formed with a laser.

16. An expandable stent for directionally delivering an active agent, the stent comprising:

a nonbiodegradable and tubular member having an exterior surface and an interior surface together defining a tubular member thickness of said tubular member, said exterior surface of said tubular member having recessed means for receiving at least one active agent, said recessed means having a depth less than said tubular member thickness.

17. The stent according to claim **16**, wherein said tubular member includes a plurality of openings passing through said tubular member thickness.

18. The stent according to claim **16**, wherein said recessed means includes a helical groove formed in said exterior surface.

19. The stent according to claim **16**, wherein said recessed means receives said at least one active agent.

20. The stent according to claim **19**, wherein said active agent is contained in a delivery matrix.

21. The stent according to claim **19**, wherein said recessed means includes a groove that is formed with a laser.

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